

# Knowledge and Technology Transfer from HEP

Manuela Cirilli  
CERN Knowledge Transfer Group



Photo: CNAO treatment room



# WHERE THE WEB WAS BORN

In the office of the director of the National Science Foundation  
Wide Web were founded.

Started in 1980 from a proposal made by Lawrence G. Roberts  
was first funded within a office created in the National  
Networking Division (NND) and was initially known as  
Computing for People (C4P).

In 1981 the first computer network was created.  
It was composed of two different networks connected  
together: JPL's (Jet Propulsion Laboratory) and the University of  
California at Berkeley.

At the end of the 1980s the network was  
expanded to include other universities and  
research centers. In 1990, the European Commission  
funded the European Concerted Action (ECA) for  
the development of the Internet.

In 1995 the American National Science Foundation  
funded the Advanced Research and Computing  
Environment (ARCE) program.



Briefing n° **12** —

## Large particle accelerators

February 2019



Ring segment of a particle accelerator  
© fotonat67 / Adobe Stock

### Summary

- Particle accelerators, like other kinds of “very large research infrastructure” (VRLI), make it possible to manage cutting-edge scientific and technological strategic issues: acquiring knowledge, enhancing research, preparing for technological breakthroughs, scientific and technological innovation.
- CERN, the European particle physics laboratory, is the world’s largest and the biggest circular particle accelerator in the world, producing the highest energies produced to date.
- A decision by the Japanese government is expected in 2019 regarding the accelerator project, the ILC, proposed since 2007 by the international scientific community.
- Thinking on the future European strategy for particle physics began in 2018 and should be presented in spring 2020. If the Japanese government confirms its interest in ILC, this European strategy must take account of this fact: a possible contribution from Europe, and particularly France, must be assessed in terms of scientific return, cost and industrial benefits.

CERN has also had a very strong societal impact via **the creation of the World Wide Web (WWW)** in 1989<sup>(21)</sup> under the leadership of Tim Berners-Lee and his collaborator Roger Cailliau. It was originally a response to researchers’ need to exchange a high volume of data simply and instantaneously for international collaborations. CERN published software

Mr. Cédric Villani, MP (National Assembly), First Vice-Chairman

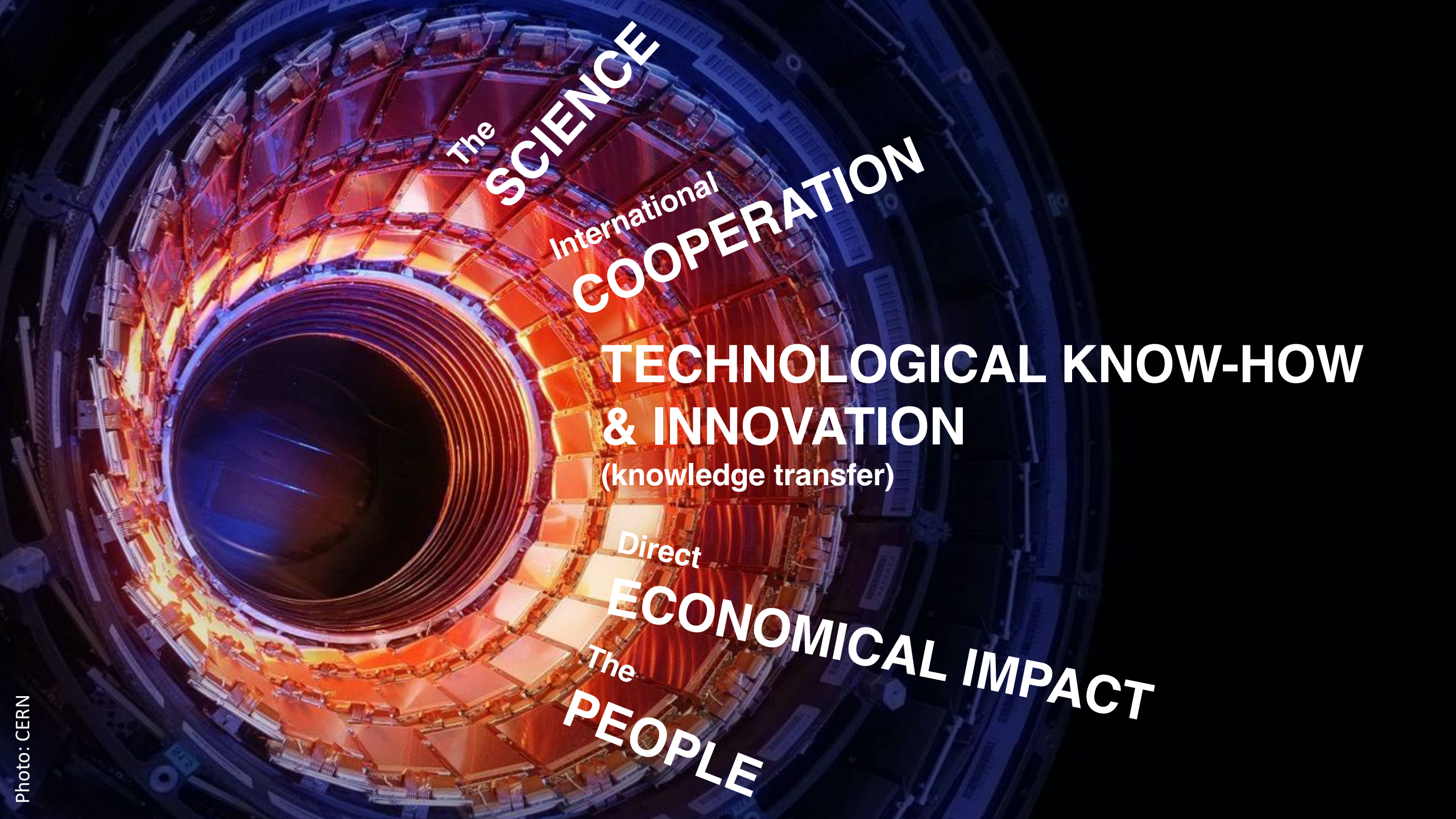




# TECHNOLOGICAL KNOW-HOW & INNOVATION

(knowledge transfer)





The  
**SCIENCE**

International

**COOPERATION**

**TECHNOLOGICAL KNOW-HOW  
& INNOVATION**

(knowledge transfer)

Direct

**ECONOMICAL IMPACT**

The  
**PEOPLE**





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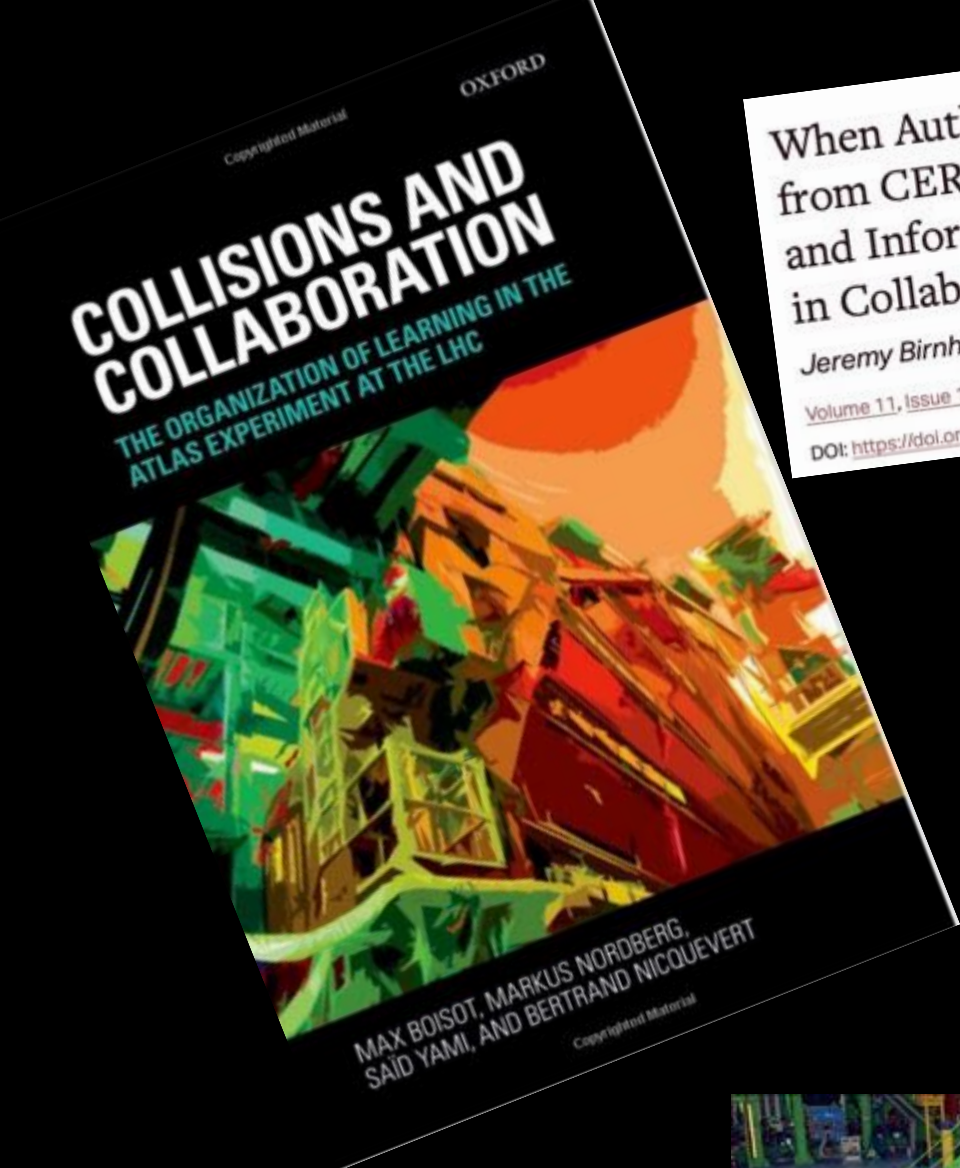
7 016

in 2021

46 704

since 2014





## When Authorship Isn't Enough: Lessons from CERN on the Implications of Formal and Informal Credit Attribution Mechanisms in Collaborative Research

Jeremy Birnholtz

Volume 11, Issue 1, Winter 2008

DOI: <https://doi.org/10.3998/3336451.0011.105>

CONCEPTUAL ANALYSIS article

Front. Res. Metr. Anal., 13 January 2021 | <https://doi.org/10.3389/frma.2020.592819>

## Collaborative Processes in Science and Literature: an In-Depth Look at the Cases of CERN and SIC

Emilia Leogrande<sup>1\*</sup> and Renato Nicassio<sup>2\*</sup>

<sup>1</sup>European Organization for Nuclear Research (CERN), Geneva, Switzerland

<sup>2</sup>Independent Researcher, Bari, Italy



The European Network for Light Ion Hadron Therapy (ENLIGHT) was established to coordinate European efforts in using ion beams for radiation therapy and to catalyse collaboration and co-operation among the different disciplines involved. ENLIGHT had its inaugural meeting in February 2002 at CERN and was funded by the European Commission for its first 3 years.

<http://cern.ch/enlight>

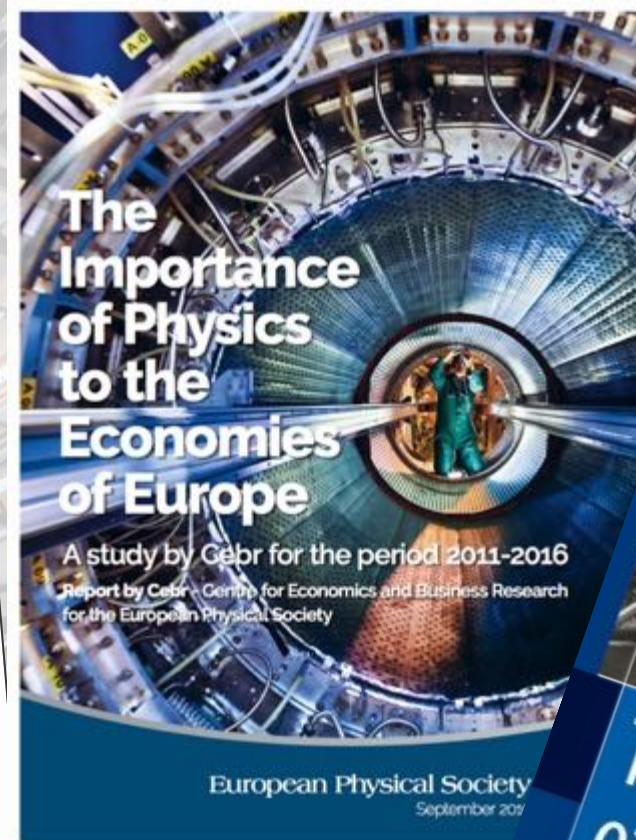




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# The Impacts of Large Research Infrastructures on Economic Innovation and on Society: Case Studies at CERN





# Cost-Benefit Analysis of the Large Hadron Collider to 2025 and beyond

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<sup>2</sup> *TIF Lab, Dipartimento di Fisica, Università di Milano and INFN, Sezione di Milano, Via Celoria 16, I-20133 Milano, Italy*

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## Abstract

Social cost-benefit analysis (CBA) of projects has been successfully applied in different fields such as transport, energy, health, education, and environment, including climate change. It is often argued that it is impossible to extend the CBA approach to the evaluation of the social impact of research infrastructures, because the final benefit to society of scientific discovery is generally unpredictable. Here, we propose a quantitative approach to this problem, we use it to design an empirically testable CBA model, and we apply it to the the Large Hadron Collider (LHC), the highest-energy accelerator in the world, currently operating at CERN. We show that the evaluation of benefits can be made quantitative by determining their value to users (scientists, early-stage researchers, firms, visitors) and non-users (the general public). Four classes of contributions to users are identified: knowledge output, human capital development, technological spillovers, and cultural effects. Benefits for non-users can be estimated, in analogy to public goods with no practical use (such as environment preservation), using willingness to pay. We determine the probability distribution of cost and benefits for the LHC since 1993 until planned decommissioning in 2025, and we find there is a 92% probability that benefits exceed its costs, with an expected net present value (NPV) of about 3 billion €, not including the unpredictable economic value of discovery of any new physics. We argue that the evaluation approach proposed here can be replicated for any large-scale research infrastructure, thus helping the decision-making on competing projects, with a socio-economic appraisal complementary to other evaluation criteria.

We determine the probability distribution of cost and benefits for the LHC since 1993 until planned decommissioning in 2025, and we find there is a **92% probability that benefits exceed its costs**, with an expected net present value of about 3 billion euro, not including the unpredictable economic value of discovery of any new physics.

## Additional reading:

Schopper, Herwig, 2016. "Some remarks concerning the cost/benefit analysis applied to LHC at CERN," *Technological Forecasting and Social Change*, Elsevier, vol. 112(C), pages 54-64.

E Pugliese, G Cimini, A Patelli, A Zaccaria, L Pietronero, A Gabrielli, *Unfolding the innovation system for the development of countries: co-evolution of Science, Technology and Production*, arXiv preprint arXiv:1707.05146

A Patelli, G Cimini, E Pugliese, A Gabrielli, *The scientific influence of nations on global scientific and technological development*, *Journal of Informetrics* 11, 1229-1237 (2017)



Over 70 companies and institutes produce accelerators for industrial applications; these organizations sell more than 1,100 industrial systems per year — almost twice the number produced for research or medical therapy — at a market value of \$2.2B.

Over \$1B of this amount is generated by the sales of accelerators for ion implantation into materials — primarily semiconductor devices — whose worldwide value of production is about \$300B.

Hamm, R. and Hamm, M. (2012). Industrial accelerators and their applications. World Scientific Publishing Co.

As of 2014 there were 42,200 accelerators worldwide:  
27,000 (64%) in industry,  
14,000 (33%) for medical purposes  
1,200 (3%) for basic research.

These figures exclude electron microscopes and x-ray tubes, and the security and defense industries.

Chernyaev, A. P. and Varzar, S. M. (2014). Particle accelerators in modern world. Physics of Atomic Nuclei, 77(10):1203–1215.

Some updated figures in Doyle, McDaniel, Hamm, The Future of Industrial Accelerators and Applications, SAND2018-5903B



# KNOWLEDGE TRANSFER through PROCUREMENT

Survey of companies involved in technology-intensive procurement contracts with CERN.

178 questionnaires analyzed, related to 503 MCHF procurement budget.

Technological learning	44%
Increased international exposure	42%
Developed new products	38%
Market learning	36%
Started new R&D teams	13%
Would have poorer technological performance without CERN	41%
Would have poorer sales performance without CERN	52%

Impact	% risposte positive/tot questionari
Technological competences	31%
Increased sales	28%
Positive return on image	25%
New partnerships/coolaborations	21%
Market learning	17%
New clients	14%
New activities	13%
Higher market shares	12%
New markets	11%





# The **HUMAN** capital

(very hard to quantify but extremely impactful for particle physics)





# Salary Differences Between Master's and Ph.D. Graduates

Average Work-Life Earnings After a Bachelor's Degree				
Major	Bachelor's Degree	Master's Degree	Doctorate Degree	% Difference in Doctorate/Master's Earnings
Biological Science	\$2,288,000	\$2,757,000	\$3,511,000	27%
Business	\$2,563,000	\$3,257,000	\$3,535,000	9%
Communications	\$2,333,000	\$2,552,000	\$3,306,000	30%
Computers and Math	\$3,044,000	\$3,541,000	\$3,890,000	10%
Education	\$1,798,000	\$2,260,000	\$2,802,000	24%
Engineering	\$3,349,000	\$3,918,000	\$4,176,000	7%
Liberal Arts	\$2,046,000	\$2,448,000	\$2,705,000	10%
Literature	\$2,083,000	\$2,444,000	\$2,755,000	13%
Physical Science	\$2,527,000	\$3,193,000	\$3,825,000	20%
Psychology	\$2,001,000	\$2,366,000	\$3,157,000	33%
Science and Engineering Related	\$2,587,000	\$2,925,000	\$3,814,000	30%
Social Science	\$2,406,000	\$2,986,000	\$3,490,000	17%
Visual Arts	\$1,966,000	\$2,227,000	\$2,545,000	14%

**Note:** This chart is for 25-64 year olds who are working full-time, year round

Source: [www.census.gov](http://www.census.gov)

**Today:**  
**> 3000 PhD students**  
**in LHC experiments**

2007-2012: 831 Fellows finished their Fellowships

The study targeted the 288 (38%) former fellows that did not have any affiliation (staff, student, user, etc.) with CERN at time of the survey

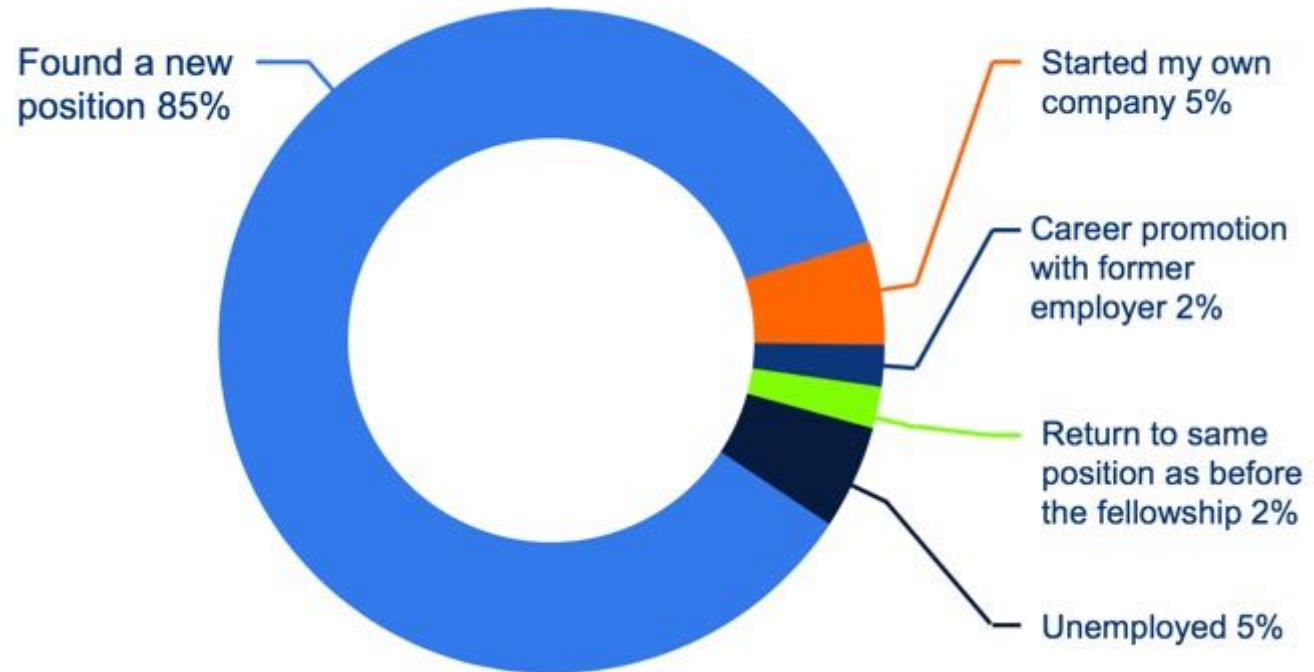
## Basic Research, Knowledge Transfer and Labor Market: Evidence from CERN's Fellowship Programs

Silvia Bruzzi\* and Giovanni Anelli\*\*

**Abstract.** Nowadays, investing in scientific research to produce knowledge is considered a main asset for winning competition and contributing to the creation of economic value for the benefit of global society. Among the different phases of R&D, basic research stands out for its very high costs, risks and a time horizon of long/very long term. Nonetheless, if well-governed, it represents the component of R&D more able to produce positive externalities at a global level. In this framework, this paper aims to focus on the wide socio-economic value generated by basic research, conceived as an irreplaceable engine of innovation. In order to measure the performance of basic research, the paper proposes to refer to the outcome of research activity, i.e. the advancement of knowledge diffused by and through people, and discuss the results of a survey developed at CERN on the past-CERN Fellows, in order to isolate the contribution of the Fellowship Programs of CERN to the Fellows' professional career, in primis in industry. Our findings testify that basic research produces a continued scientific 'fertilisation effect' of the global economic system, contributing to the creation of high skilled and professionalized human resources to the benefit of industry and other employers, so generating positive externalities wider than those measured in terms of patents and publications, the metrics traditionally used to measure the performance of research.

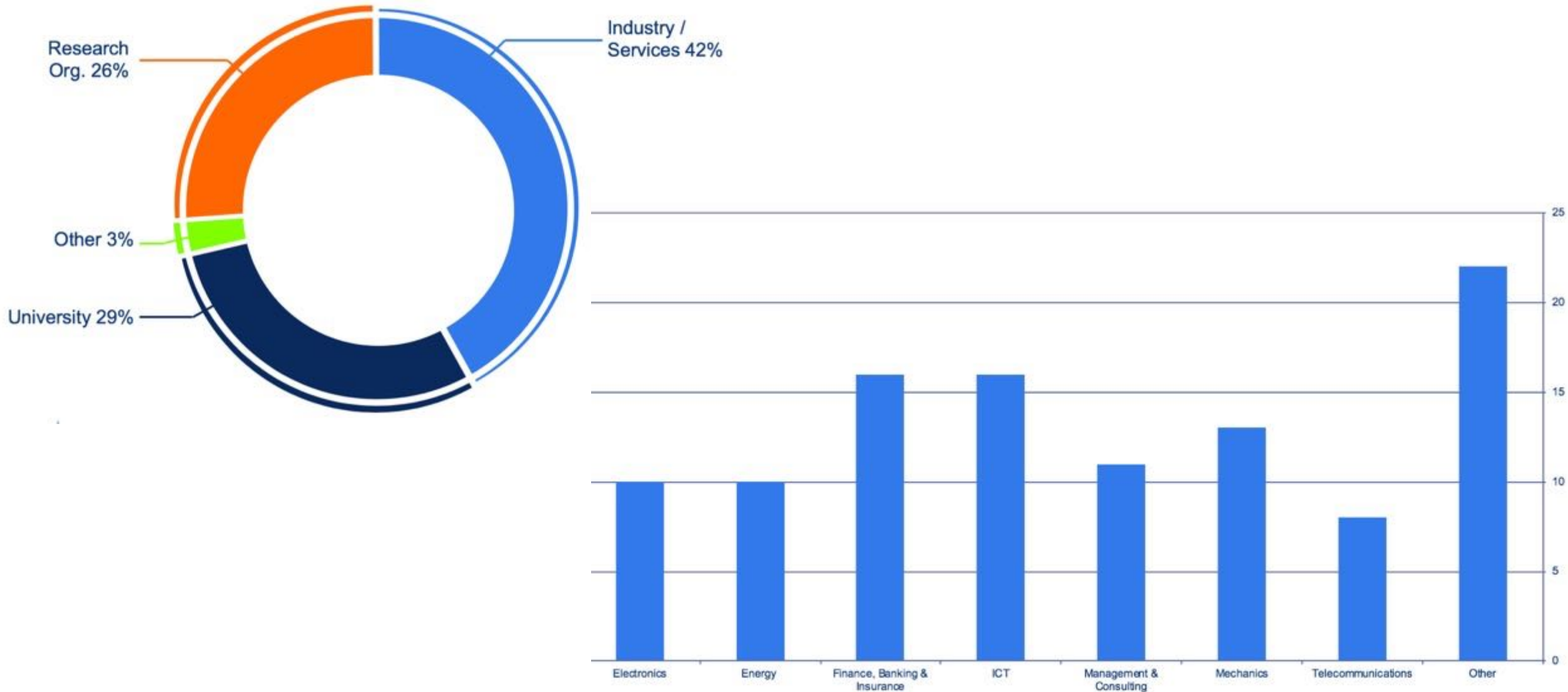
**Keywords:** Basic Research; Knowledge Transfer; Labor Market; CERN.

First Position after Fellowship



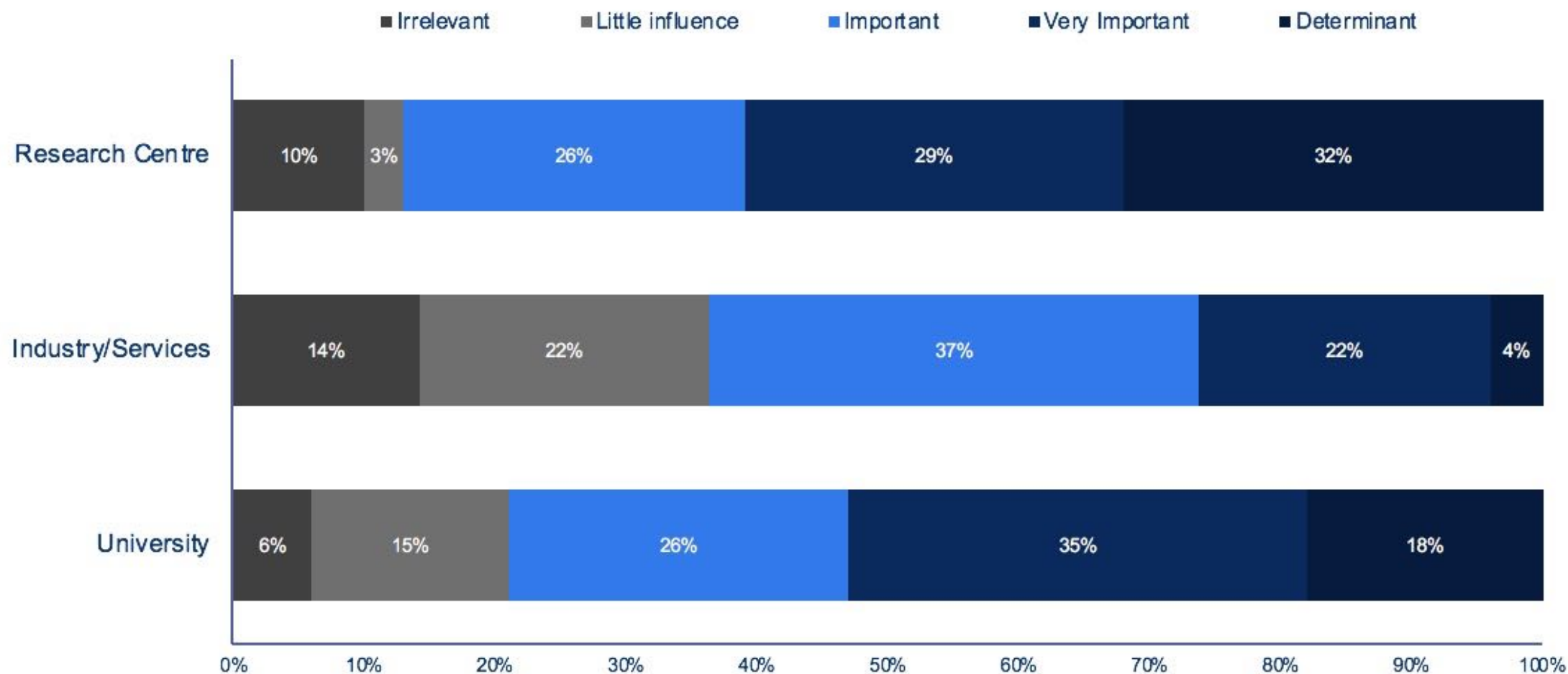


# First Position after Fellowship



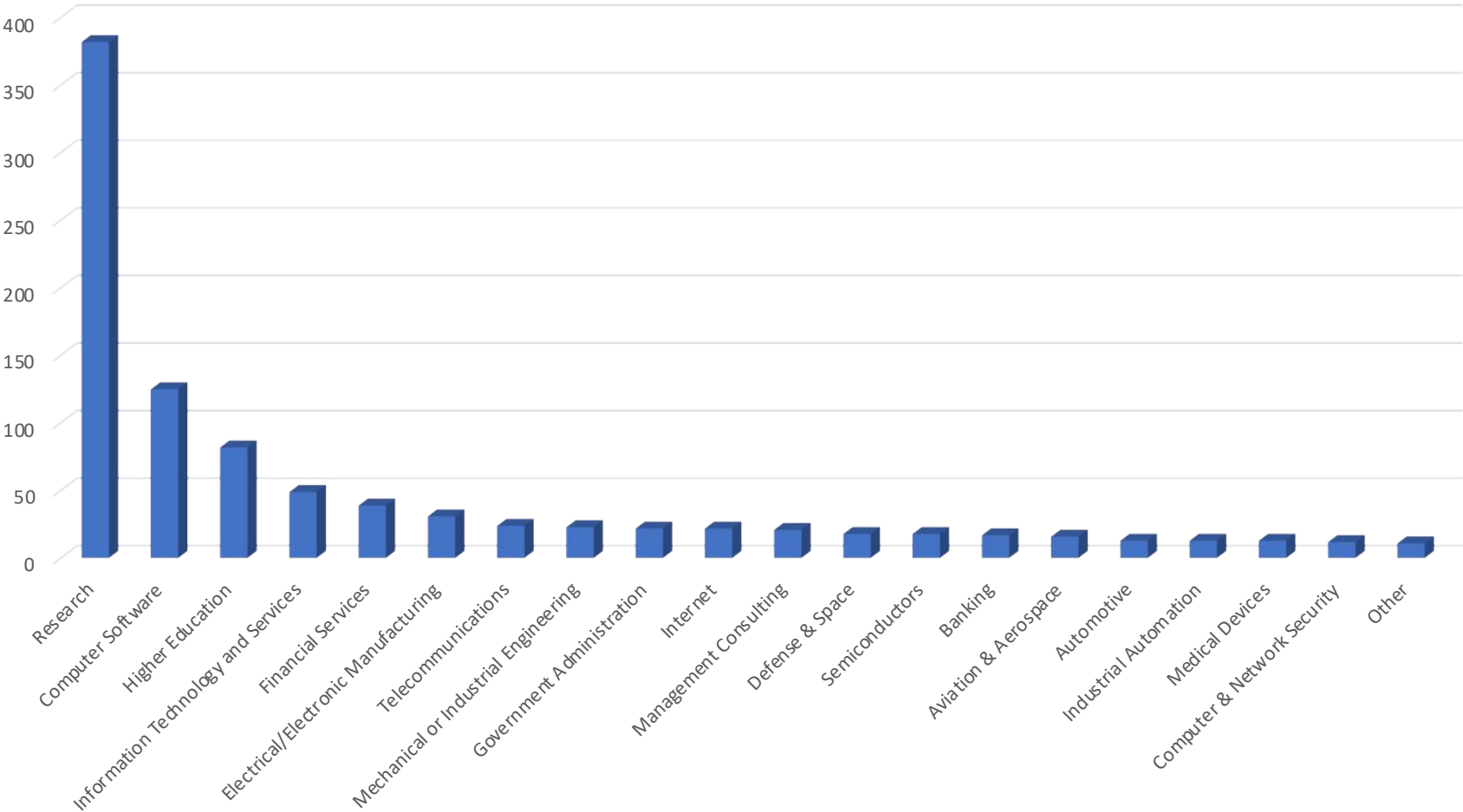
# First Position after Fellowship

How important was the CERN fellowship to secure your first position after the fellowship?





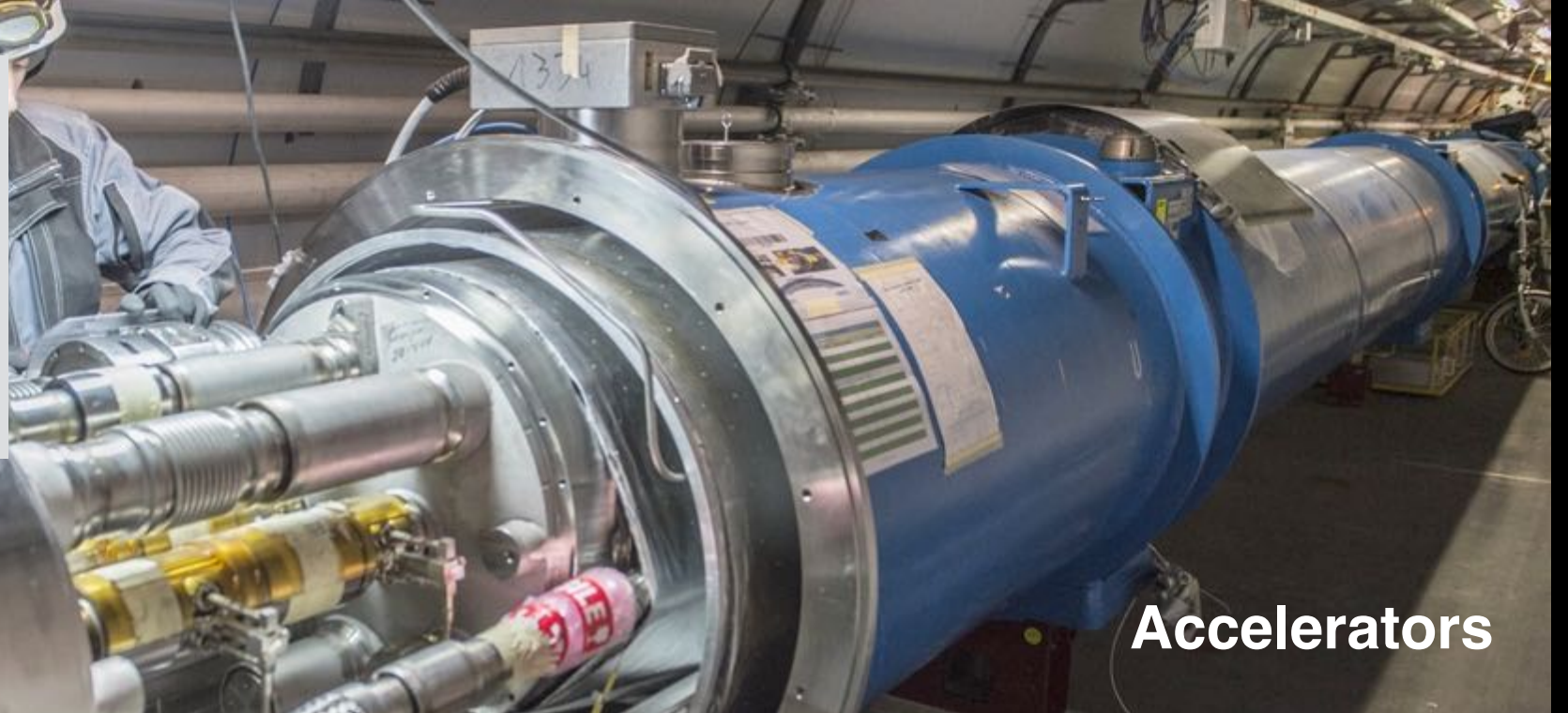
# Top Twenty Industry Sectors of CERN Alumni Community:



<https://alumni.cern/signup>



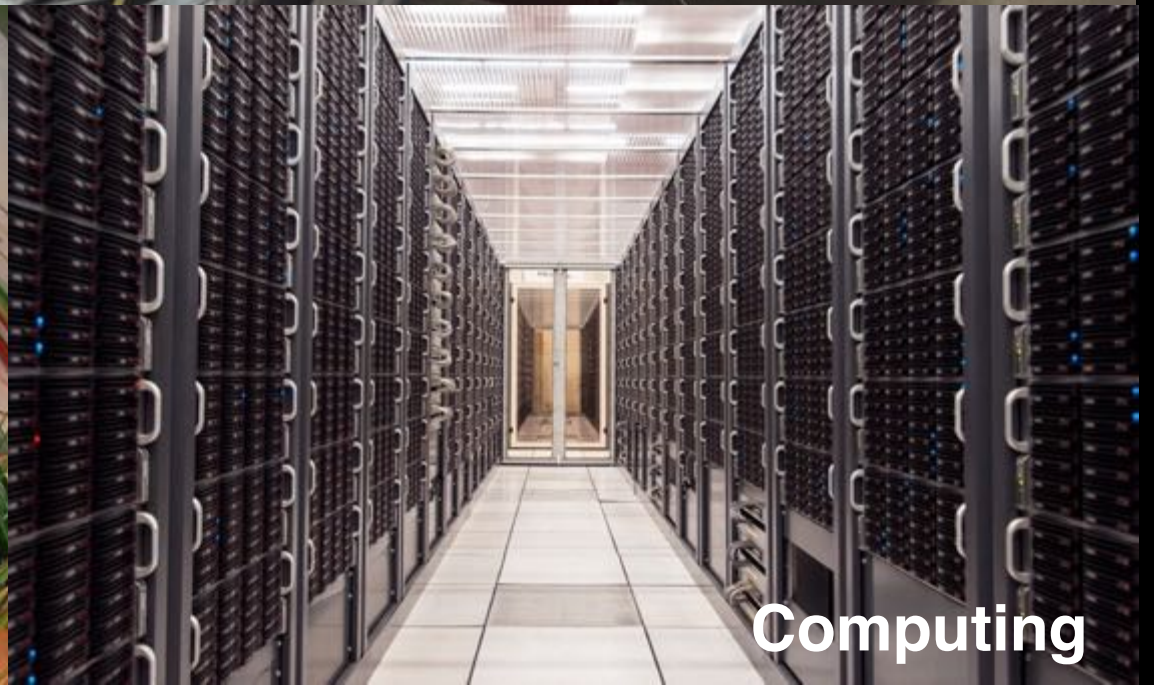
# Technologies and know-how



**Accelerators**



**Detectors**



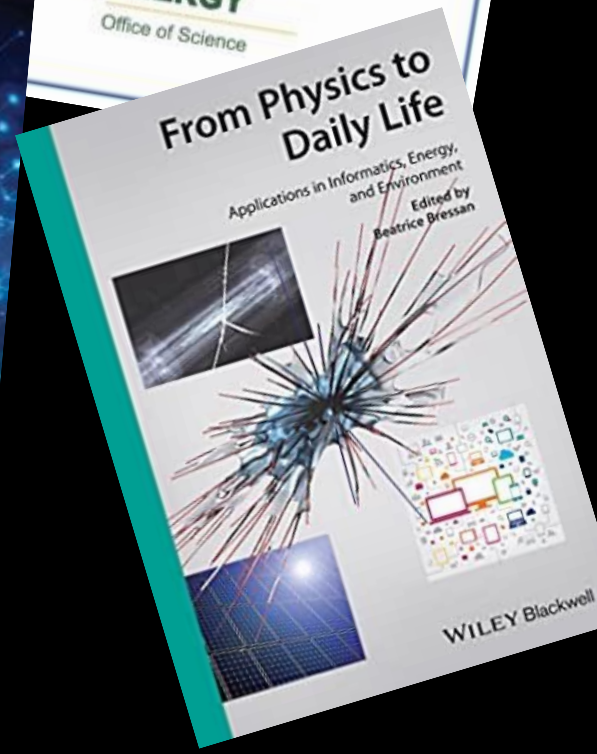
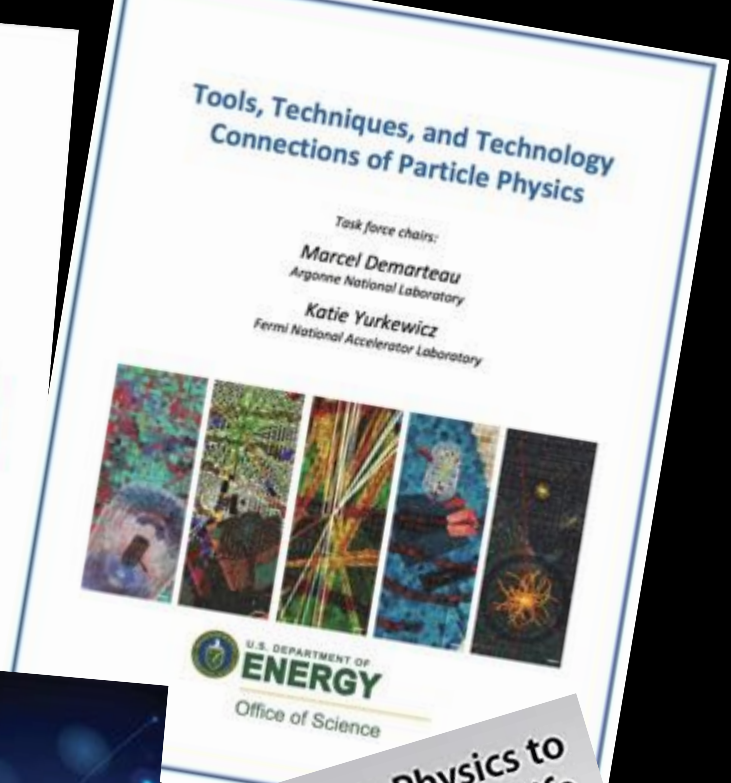
**Computing**



A word cloud featuring various scientific and technological terms. The words are arranged in a circular pattern, with some terms appearing more frequently than others. The colors of the text range from white to bright yellow.

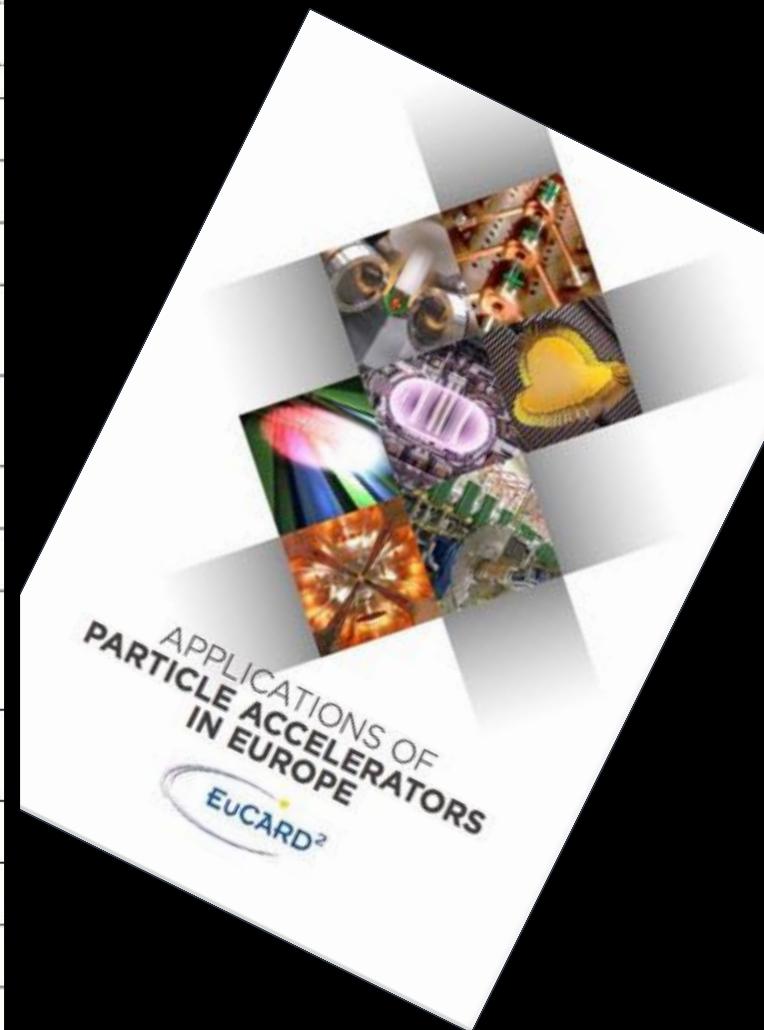
sound reproduction  
data management  
astronauts' radiation exposure  
testing satellite components  
understanding turbulence  
medical implants  
homeland security  
curing of epoxies and plastics  
x-ray diffractometry  
radiology  
medical radioisotopes  
rad-hard electronics  
simulations  
optimised irrigation systems  
safety  
powering complex biological simulations  
analysis of satellite data  
volcano tomography  
sealing food packages  
autonomous vehicles  
smoke detectors  
hadron therapy  
MRI  
cleaner air and water  
cargo screening  
computer chips manufacturing  
studying the retina  
medical dosimetry  
material science  
ink curing  
WWW  
space applications  
spacecraft shielding  
finding oil, gas, water  
scientific linux  
geological dating  
shrink wrap  
non-destructive testing  
ion implantation  
PET  
terrestrial reproduction of space radiation  
industry 4.0  
open hardware  
industrial control systems  
treatment planning systems  
digital data preservation  
nuclear waste transmutation  
drug development  
power transmission  
isotope production  
cultural heritage  
food sterilization  
medical imaging  
medical equipment sterilization







Area	Application	Beam	Accelerator	Beam energy/MeV	Beam current/ mA	Number
Medical	Cancer therapy	e	linac	4-20	$10^{-2}$	>14000
		p	cyclotron, synchrotron	250	$10^{-6}$	60
		C	synchrotron	4800	$10^{-7}$	10
	Radioisotope production	p	cyclotron	8-100	1	1600
Industrial	Ion implantation	B, As, P	electrostatic	< 1	2	>11000
	Ion beam analysis	p, He	electrostatic	<5	$10^{-4}$	300
	Material processing	e	electrostatic, linac, Rhodatron	$\leq 10$	150	7500
	Sterilisation	e	electrostatic, linac, Rhodatron	$\leq 10$	10	3000
Security	X-ray screening of cargo	e	linac	4-10	?	100?
	Hydrodynamic testing	e	linear induction	10-20	1000	5
Synchrotron light sources	Biology, medicine, materials science	e	synchrotron, linac	500-10000		70
Neutron scattering	Materials science	p	cyclotron, synchrotron, linac	600-1000	2	4
Energy - fusion	Neutral ion beam heating	d	electrostatic	1	50	10
	Heavy ion inertial fusion	Pb, Cs	Induction linac	8	1000	Under development
	Materials studies	d	linac	40	125	Under development
Energy - fission	Waste burner	p	linac	600-1000	10	Under development
	Thorium fuel amplifier	p	linac	600-1000	10	Under development
Energy - bio-fuel	Bio-fuel production	e	electrostatic	5	10	Under development
Environmental	Water treatment	e	electrostatic	5	10	5
	Flue gas treatment	e	electrostatic	0.7	50	Under development

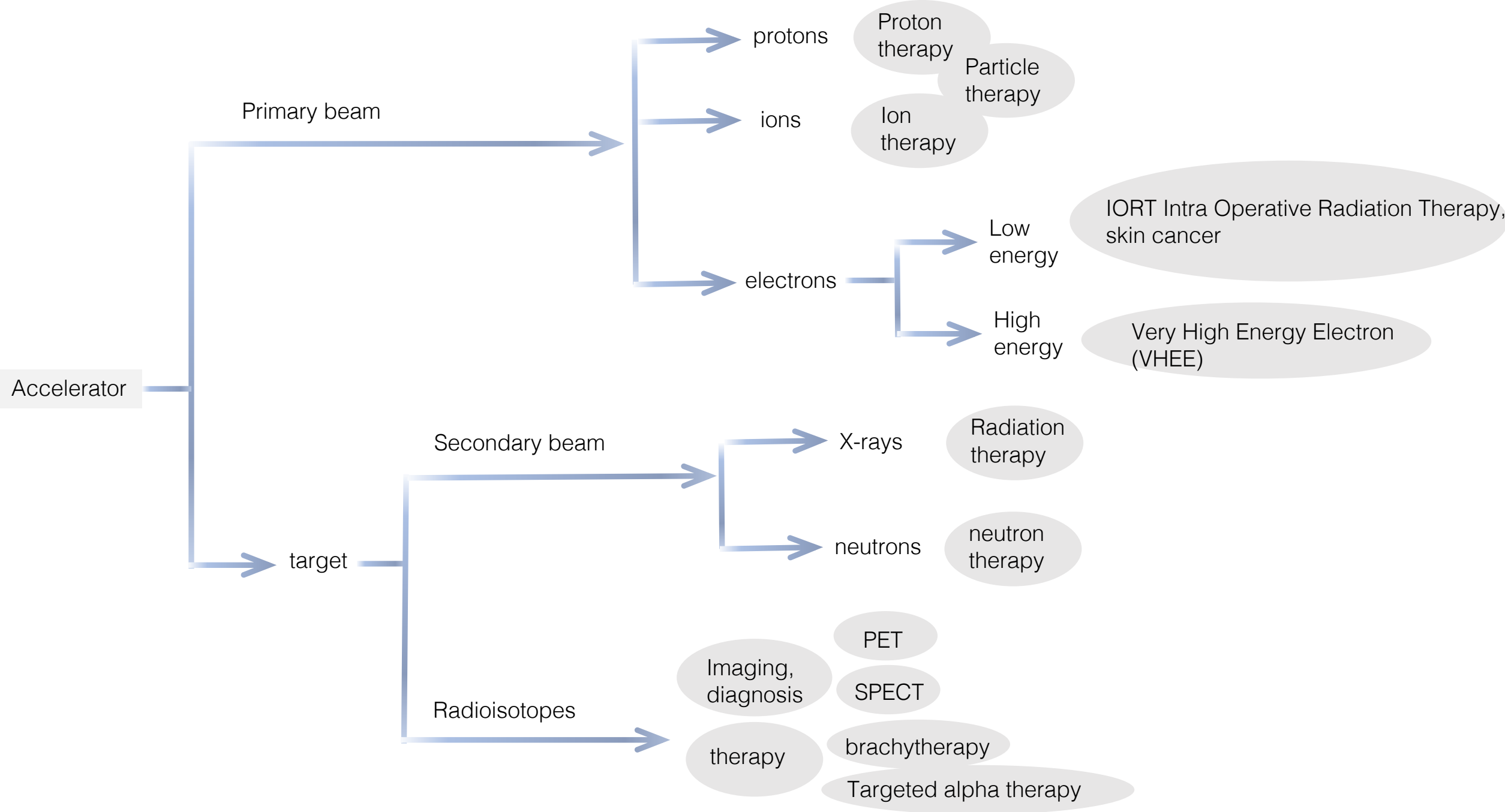


# X-Rays



**1895**





# Radiotherapy





# Status of Radiation Therapy Equipment

**155** **7602**

Countries

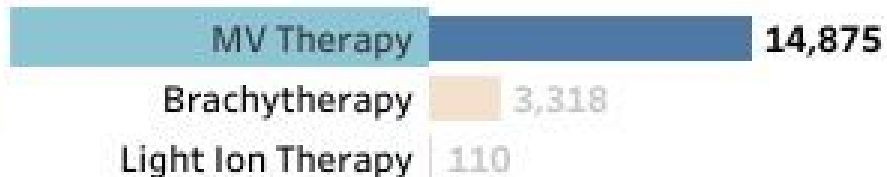
RT Centres

**14875**

MV Therapy

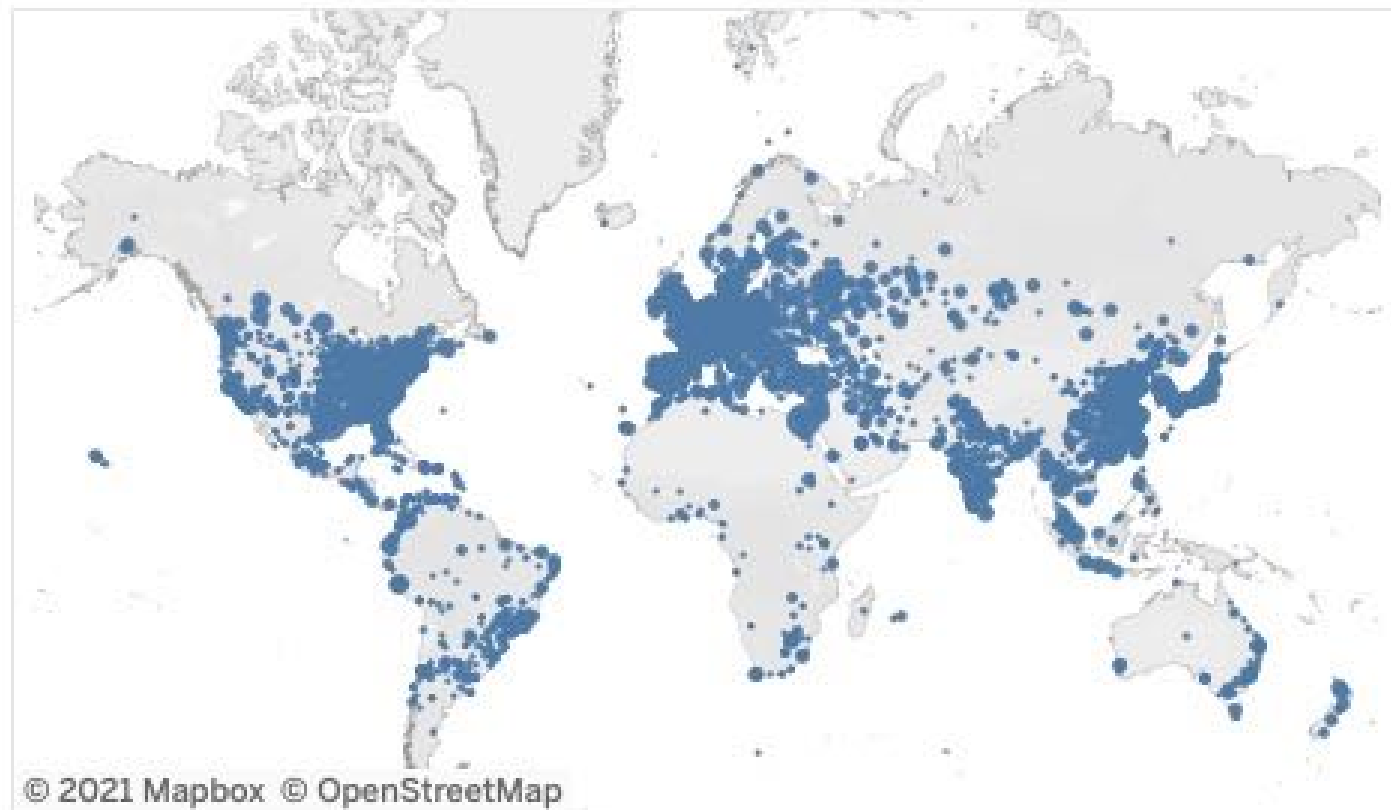
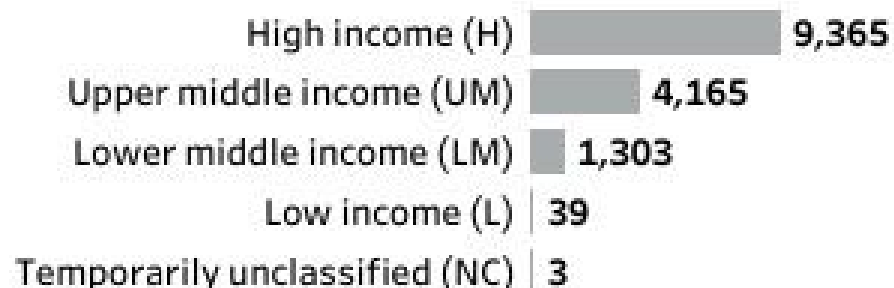
## Equipment type

(Updated on : 23/06/2021 09:19:53)



## Equipment per income groups

(Updated on : 23/06/2021 09:19:53)



IAEA

DIRAC

Directory of  
Radiotherapy Centres

# Status of Radiation Therapy Equipment

**155** **7602**

Countries

RT Centres

**14875**

MV Therapy

STELLA Collaboration formed to address the lack of radiotherapy in challenging environments. Supported by ICEC, UK STFC, Lancaster and Oxford University, CERN, users in LMICs

14,875

(Updated on : 23/06/2021 09:19:53)



High income (H)	9,365
Upper middle income (UM)	4,165
Lower middle income (LM)	1,303
Low income (L)	39
Temporarily unclassified (NC)	3



IAEA

DIRAC

Directory of  
Radiotherapy Centres



## Berkeley

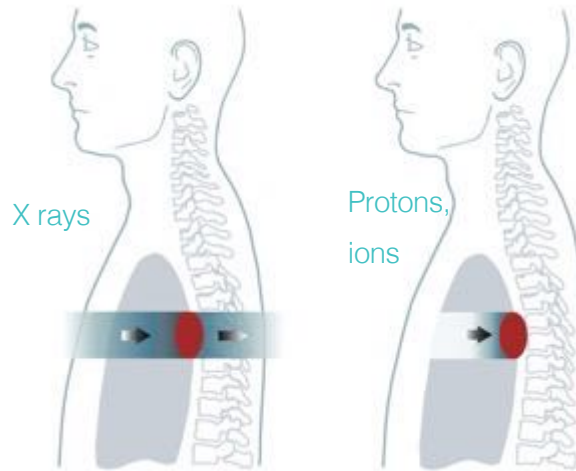
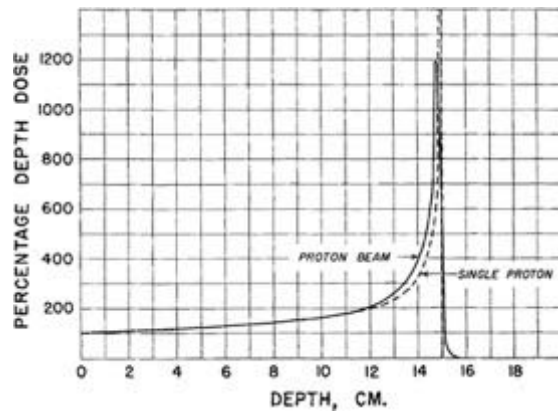
1931 Invention of cyclotron (Ernest Lawrence)

1946 RR Wilson published his seminal paper on particle therapy

1952 First biological investigation with accelerated nuclei (C Tobias and JH Lawrence)

1954 First therapeutic exposure of humans to protons and alphas (Tobias and JH Lawrence)

1975 Clinical trials with accelerated light ions at LBL (Castro)



## Gustav Werner Institute and Theodor Svedberg Laboratory

1949 Synchrocyclotron at the Gustav Werner Institute (Uppsala)

1950s Pre-therapeutic physical experiments with high energy protons (B. Larsson)

1957 First patient treated with proton beam



# Status of Radiation Therapy Equipment

**20** **106**

Countries

RT Centres

**110**

Light Ion Therapy

## Equipment type

(Updated on : 23/06/2021 09:19:53)

MV Therapy 14,875

Brachytherapy 3,318

Light Ion Therapy 110

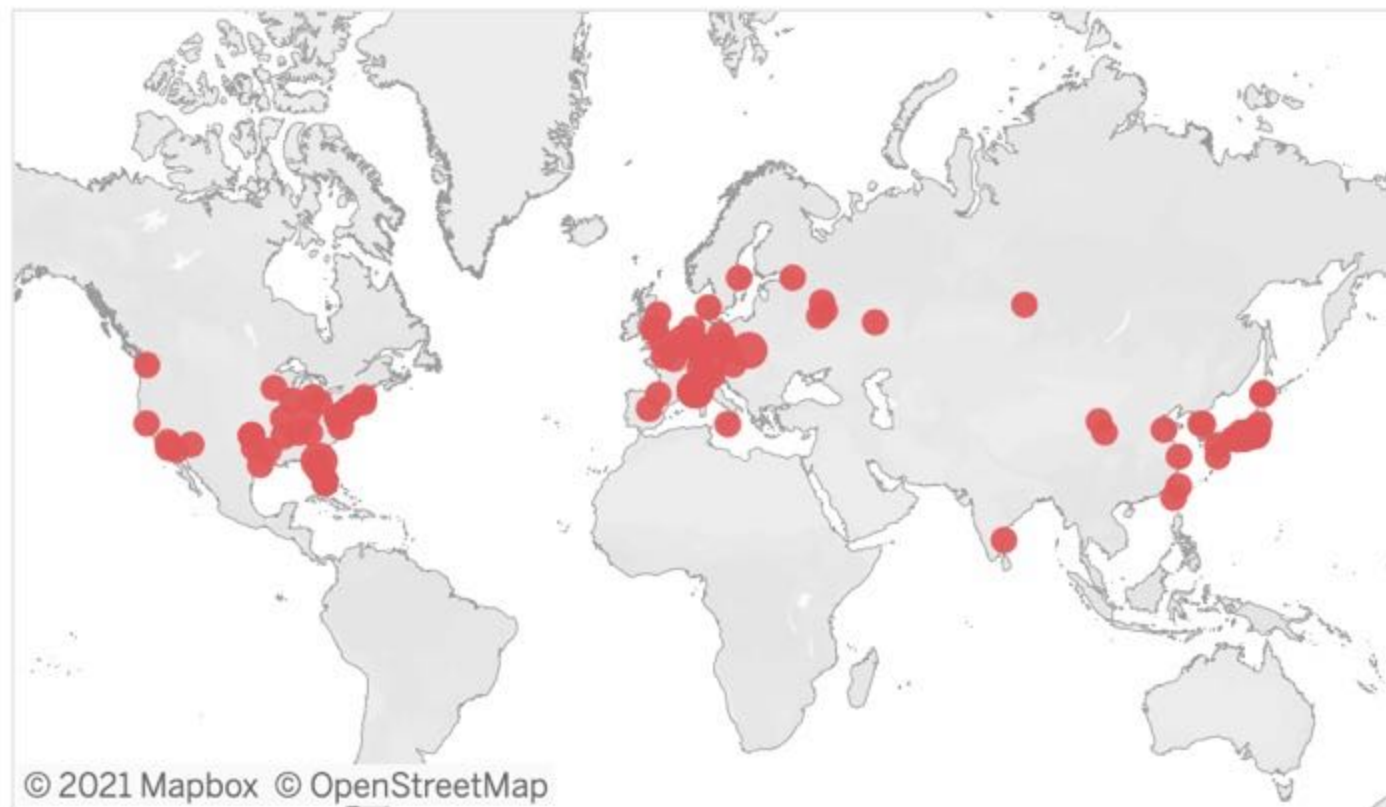
## Equipment per income groups

(Updated on : 23/06/2021 09:19:53)

High income (H) 99

Upper middle income (UM) 10

Lower middle income (LM) 1



IAEA

DIRAC

Directory of  
RAdiotherapy Centres



# Protons: the LINAC way

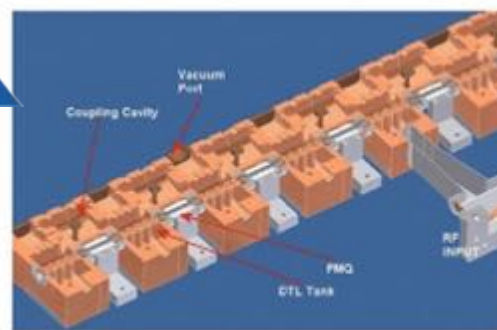
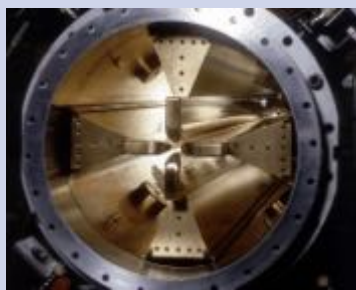


Fig. 4. TOP-IMPLART SCDTL structure: (left) schematic (right) 18-24 MeV booster built for the SPARKLE Company.

**1990**  
RFQ2  
200 MHz  
0.5 MeV /m  
Weight :1200kg/m  
Ext. diametre : ~45 cm

**2007**  
LINAC4 RFQ  
352 MHz  
1MeV/m  
Weight : 400kg/m  
Ext. diametre : 29 cm

**2014**  
HF RFQ  
750MHz  
2.5MeV/m  
Weight : 100 kg/m  
Ext. diametre : 13 cm



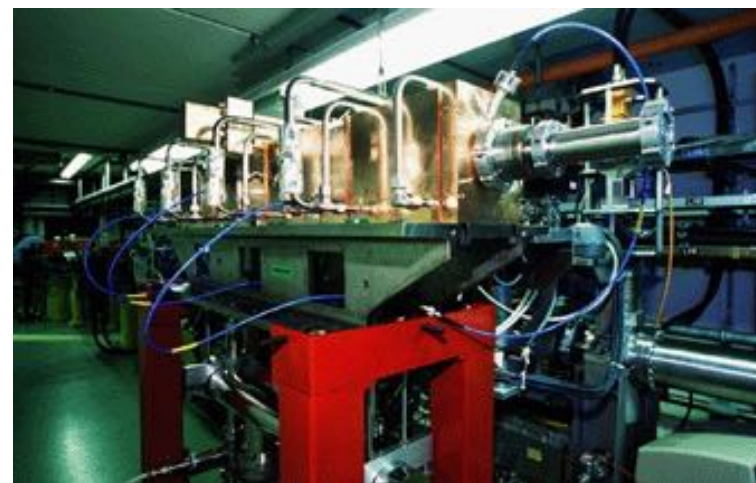
## Compact High-Frequency Radio Frequency Quadrupole (RFQ)

M. Vretenar, A. Dallochio, V. A. Dimov, M. Garlasché, A. Grudiev, A. M. Lombardi, S. Mathot, E. Montesinos, M. Timmins, "A Compact High-Frequency RFQ for Medical Applications", in Proc. LINAC2014, Geneva, Switzerland, September 2014



## TOP IMPLART

L. Picardi, C. Ronsivalle, A. Vignati, Progetto del TOP Linac, ENEA Technical Report RT/INN/97/17 (in Italian) (1997)  
C. Ronsivalle, M. Carpanese, C. Marino, G. Messina, L. Picardi, S. Sandri, E. Basile, B. Caccia, D.M. Castelluccio, E. Cisbani, S. Frullani, F. Ghio, V. Macellari, M. Benassi, M. D'Andrea, L. Strigari, The TOP-IMPLART project, Eur. Phys. J. Plus 126: 68 (2011) 1–15, <http://dx.doi.org/10.1140/epjp/i2011-11068-x>.



## Linac BOoster (LIBO)

U. Amaldi et al., LIBO: a 3 GHz proton linac booster of 200 MeV for cancer treatment, in Proceedings of the XIX International Linear Accelerator Conference, Chicago, (1998), p. 633U. Amaldi et al., "LIBO-a linac booster for protontherapy: construction and test of a prototype," Nucl. Instrum. Methods Phys. Res. A, vol. 521, pp. 512-529, 2004.

# Toward clinical proton therapy LINACs

The RFQ accelerating structure entirely manufactured by AVO (under CERN licence) has completed the Factory Acceptance Testing protocols and is RF tuned.

The RFQ is ready to be installed into the beamline at STFC (Daresbury) AVO integration site in the next weeks.



CERN proton therapy RFQ (5 MeV / 2m)



TOP IMPLART under development and construction by ENEA in collaboration with the Italian Institute of Health (ISS) and the Oncological Hospital Regina Elena-IFO.

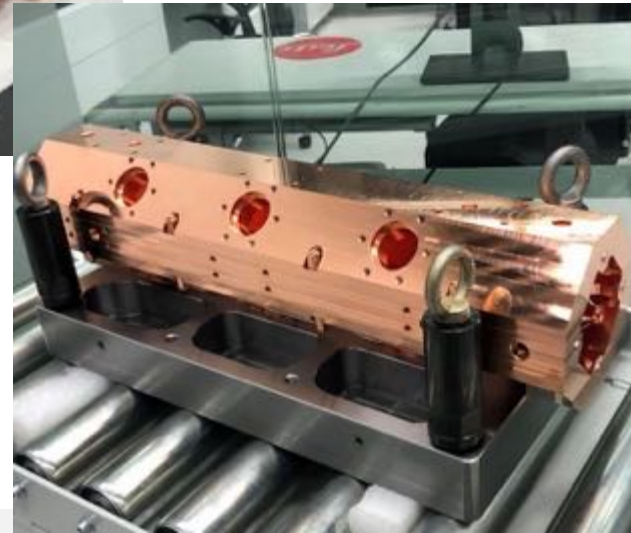
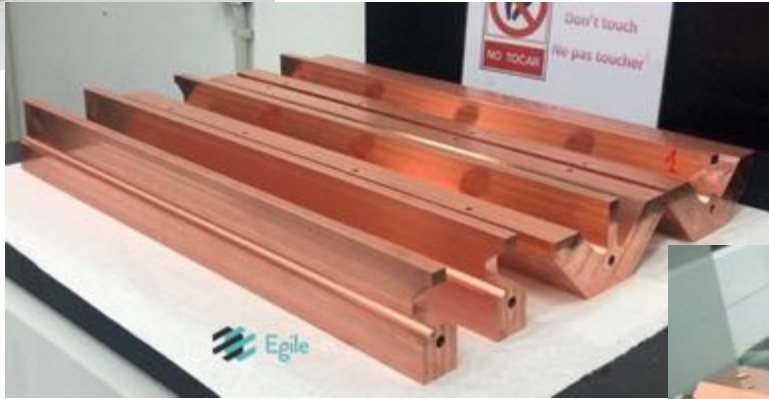
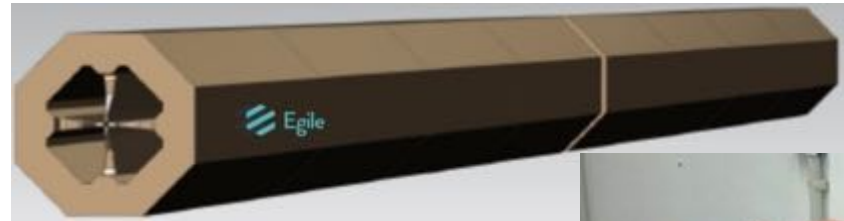
Status in March 2021\*: running at 55.5 MeV

\*<http://www.frascati.enea.it/accelerators/Sito/TopImplartStatus&Schedules/index.htm>

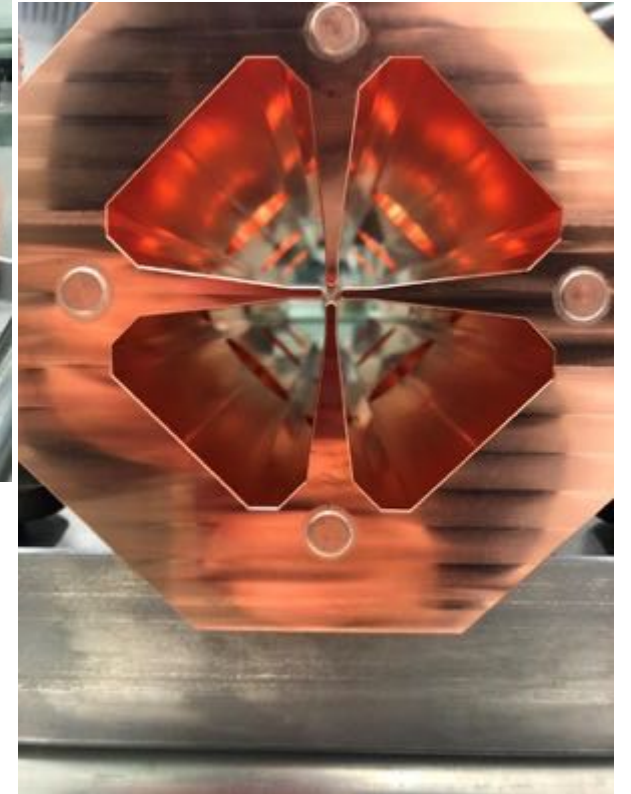
ERHA (Enhanced Radiotherapy with Hadrons) is the innovative proton therapy system being developed by LinearBeam for the treatment of tumors. Collaboration with (among others) ENEA, INFN.



# Next challenge: Carbon and other ions

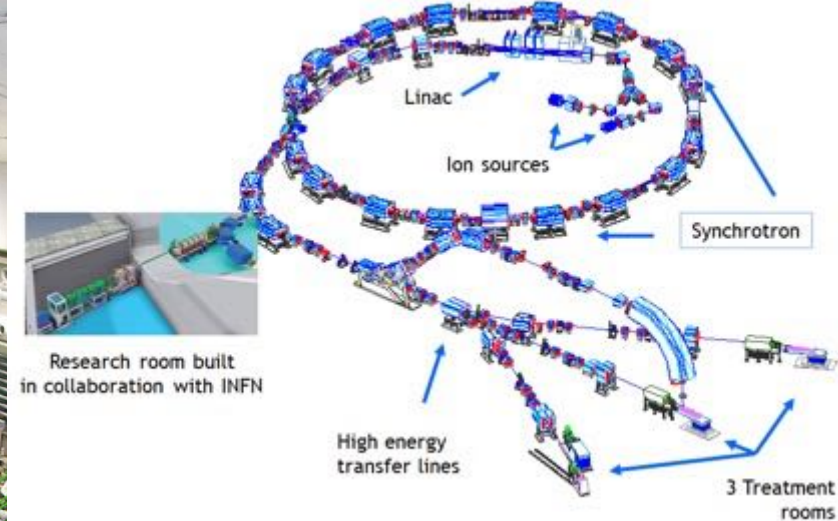


First (of 4 sections) completed



Collaboration CERN-CIEMAT-CDTI-Spanish industry  
2.0 m long  
750 MHz  
Will deliver Carbon (or Helium) at 5 MeV (total energy)  
Designed at CERN built in Spanish Industry





Sources  
to generate

1 RF cavity  
to accelerate

16 Dipoles  
to bend

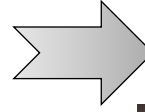
20 Correctors  
to steer

Linac  
to pre-  
accelerate

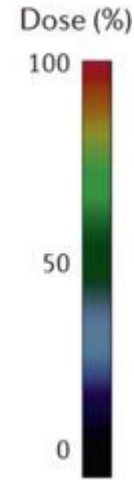
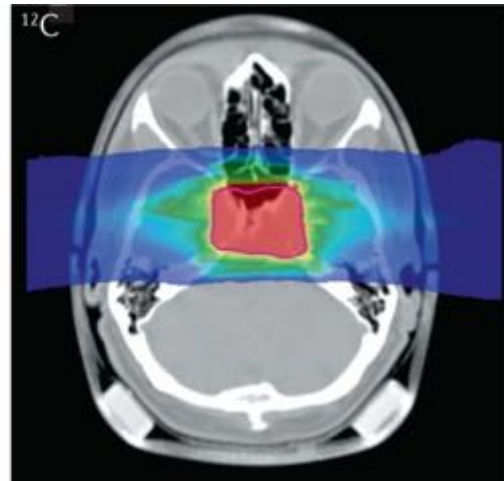
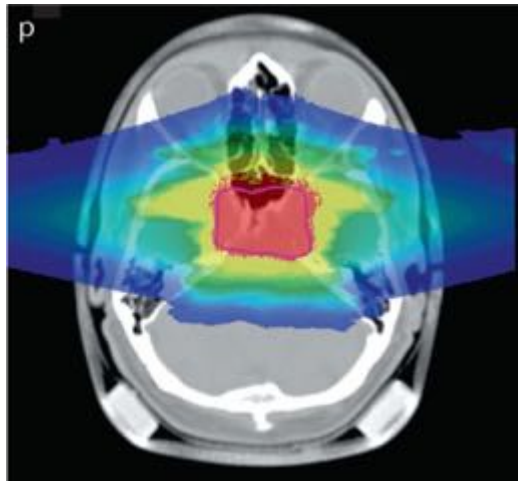
24 Quadrupoles  
to focus



From pioneering rasterscanning & carbon ion pilot project @



440 patients  
1998-2008



The image shows an optimized plan with two opposite fields for a chordoma patient using protons (left) or <sup>12</sup>C ions (right).



Courtesy HIT/Heidelberg

Since 2009\*:  
2841 patients with p  
3793 patients with C-ion

## PROTON-ION MEDICAL MACHINE STUDY (PIMMS) PART II

Accelerator Complex Study Group\*  
supported by the Med-AUSTRON, Onkologie-2000 and the TERA Foundation  
and hosted by CERN

### ABSTRACT

The Proton-Ion Medical Machine Study (PIMMS) group was formed following an agreement between the Med-AUSTRON (Austria) and the TERA Foundation (Italy) to combine their efforts in the design of a cancer therapy synchrotron capable of accelerating either light ions or protons. CERN agreed to support and host this study in its PS Division. A close collaboration was also set up with GSI (Germany). The study group was later joined by Onkologie-2000 (Czech Republic). Effort was first focused on the theoretical understanding of slow extraction and the techniques required to produce a smooth beam spill for the conformal treatment of complex-shaped tumours with a sub-millimetre accuracy by active scanning with proton and carbon ion beams. Considerations for passive beam spreading were also included for protons. The study has been written in two parts. The more general and theoretical aspects are recorded in Part I and the specific technical design considerations are presented in the present volume, Part II. An accompanying CD-ROM contains supporting publications made by the team and data files for calculations. The PIMMS team started its work in January 1996 in the PS Division and continued for a period of four years.

\*Full-time members: L. Badano<sup>1)</sup>, M. Benedikt<sup>2)</sup>, P.J. Bryant<sup>2)</sup> (Study Leader), M. Crescenti<sup>1)</sup>, P. Holy<sup>3)</sup>, A. Maier<sup>2)\*4)</sup>, M. Pullia<sup>1)</sup>, S. Reimoser<sup>2)\*4)</sup>, S. Rossi<sup>1)</sup>,  
Part-time members: G. Borri<sup>1)</sup>, P. Knaus<sup>1)\*2)</sup>  
Contributors: F. Gramatica<sup>1)</sup>, M. Pavlovic<sup>4)</sup>, L. Weisser<sup>5)</sup>

1) TERA Foundation, via Paccini, 11, I-28100 Novara.

2) CERN, CH 1211 Geneva-23.

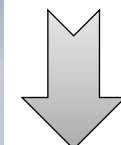
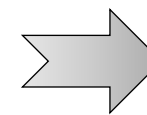
3) Oncology-2000 Foundation, Na Morani 4, CZ-12808 Prague 2.

4) Med-AUSTRON, c/o RIZ, Prof. Dr. Stephan Korenstr.10, A-2700 Wr. Neustadt.

5) Sommer & Partner Architects Berlin (SPB), Hardenbergplatz 2, D-10623 Berlin.

Geneva, Switzerland  
May 2000

From PIMMS @



fondazione CNAO



MedAustron



# Patient treatment at MedAustron



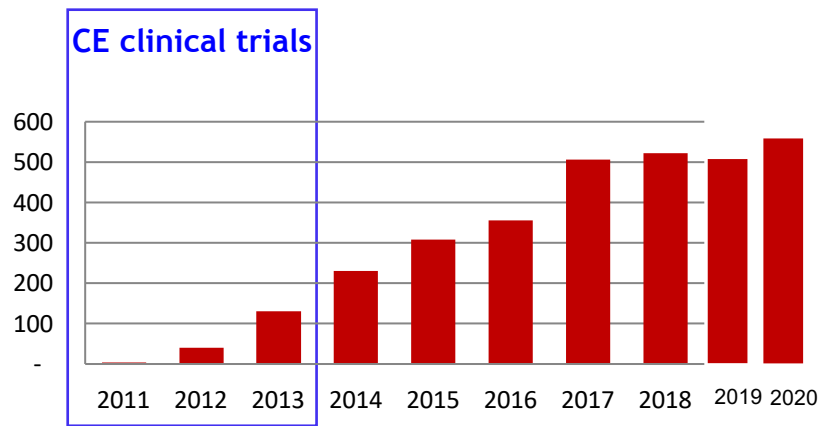
Since 2016:  
1174 Patients  
30600 Single Fractions

<b>CNS</b>	<b>28%</b>
<b>Head &amp; Neck</b>	<b>20%</b>
<b>Pediatrics</b>	<b>15%</b>
<b>Re-Irradiation</b>	<b>15%</b>
<b>Sarcoma</b>	<b>9%</b>
<b>Skull Base</b>	<b>7%</b>
<b>Prostate</b>	<b>3%</b>
<b>Gastrointestinal (upper)</b>	<b>2%</b>
<b>Gastrointestinal (lower)</b>	<b>&lt;1%</b>
<b>Gynecological Tumors</b>	<b>&lt;1%</b>
<b>Urogenital Tumors</b>	<b>&lt;1%</b>
<b>Breast/Mamma-Ca</b>	<b>&lt;1%</b>

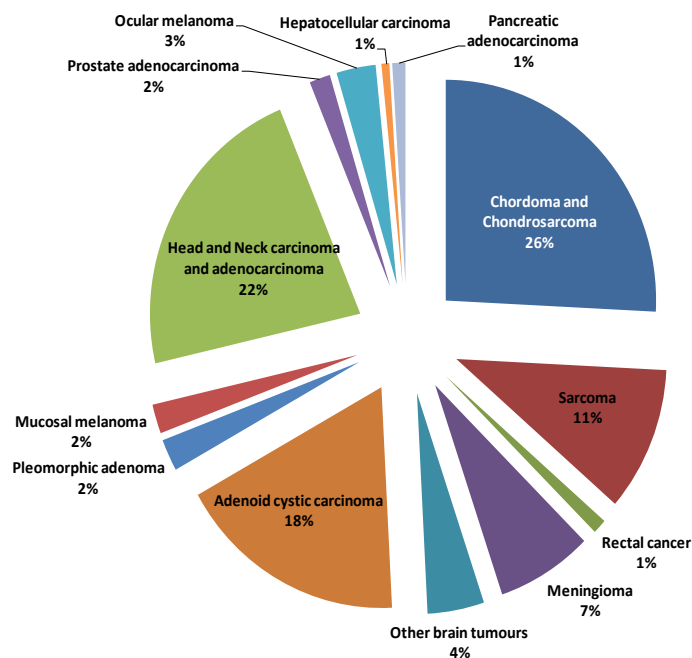
Values October 2021 • values rounded

# Patient treatment at CNAO

Since 2011:  
3700 Patients  
55% C-ions  
45% Protons



Patients per year



Non oncological application: ventricular arrhythmia  
(Collaboration with San Matteo Hospital, Pavia)  
Published: European Journal of Heart Failure

> [Eur J Heart Fail.](#) 2020 Nov 12. doi: 10.1002/ejhf.2056. Online ahead of print.

## The First-in-Man Case of Non-invasive Proton Radiotherapy to Treat Refractory Ventricular Tachycardia in Advanced Heart Failure

Veronica Dusi <sup>1 2</sup>, Viviana Vitolo <sup>3</sup>, Laura Frigerio <sup>1 4</sup>, Rossana Totaro <sup>1 4</sup>, Adele Valentini <sup>5</sup>, Amelia Barcellini <sup>3</sup>, Alfredo Mirandola <sup>3</sup>, Giovanni Battista Perego <sup>6</sup>, Michela Coccia <sup>2</sup>, Alessandra Greco <sup>4</sup>, Stefano Ghio <sup>4</sup>, Francesca Valvo <sup>3</sup>, Gaetano Maria De Ferrari <sup>7</sup>, Massimiliano Gnechi <sup>1 2</sup>, Luigi Oltrona Visconti <sup>4</sup>, Roberto Rordorf <sup>1 4</sup>

Affiliations + expand

PMID: 33179329 DOI: [10.1002/ejhf.2056](#)



# Challenges for next-generation ion-therapy machines

Cost-effective technologies

Reduced footprint

New treatment regimes (e.g. FLASH, microbeams) and fractionation schedules

Multi-ions

Radiobiology research integrated in the facility



Vozenin et al  
Clin Cancer Res 2018



**Fig. 1.** Temporal evolution of the treated lesion: (a) before treatment; the limits of the PTV are delineated in black; (b) at 3 weeks, at the peak of skin reactions (grade 1 epithelitis NCI-CTCAE v 5.0); (c) at 5 months.

First human patient – skin cancer treated with 10 MeV-range electrons

# (European) technologies for next-generation ion-therapy machines

Many challenges in common with those for future particle physics facilities. Various initiatives starting/on-going:

The Next Ion Medical Machine Study (NIMMS) collaborative study coordinated by CERN

H2020 HITRIplus project (CNAO, Bevatech, CEA, CERN, CIEMAT, Cosylab, GSI, INFN, MedAustron, PSI, Riga, UKGM, UKHD/HIT, Malta, Marburg, Uppsala, Wigner)

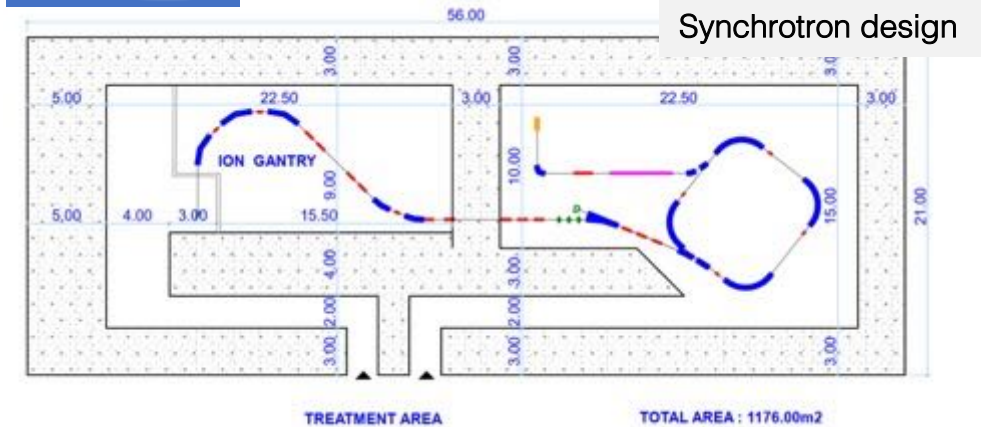
EC-funded study for SEEIIST (CERN, GSI)

Ion superconducting gantry (CERN, CNAO, MedAustron, INFN)

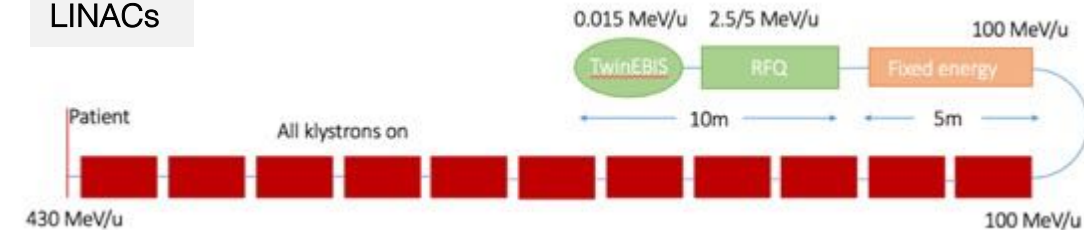
Ion linac injector (CERN, CIEMAT)

Dedicated WP on magnets for medical accelerators in H2020 IFAST project (GSI, BI, BT, CERN, HIT, CERN, CEA, INFN, CIEMAT, Wigner, UU, PSI, Scanditronix, Elytt, SigmaPhi)

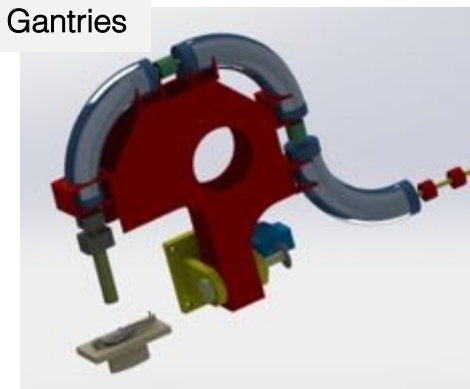
SIG Superconducting Ion Gantry project (INFN)



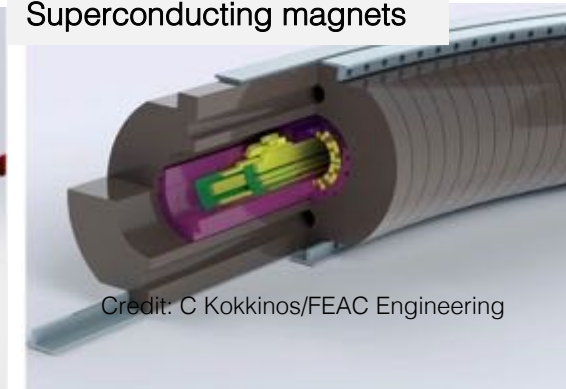
LINACs



Gantries



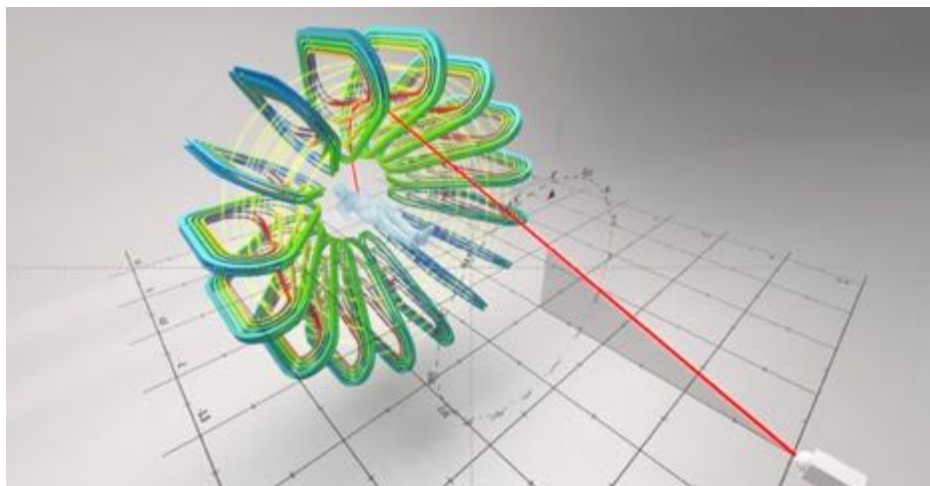
Superconducting magnets



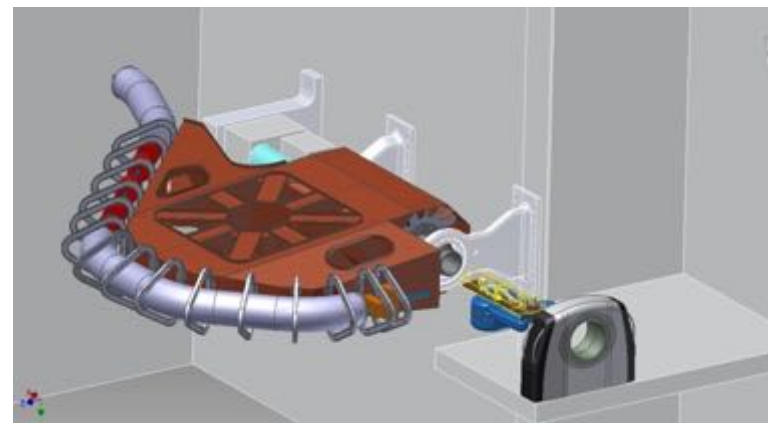


# R&D on gantries

GaToroid: A Novel Concept for a Superconducting Compact and Lightweight Gantry for Hadron Therapy



Collaboration CNAO-INFN-CERN-MedAustron  
under discussion: start 2021, 4 years project



**SIGRUM**

Superconducting Ion  
Gantry with Riboni's  
Unconventional Mechanics



Approved for  
financing



CSN5 – Call 2021

**SIG**

**Superconducting Ion Gantry**

Lucio Rossi

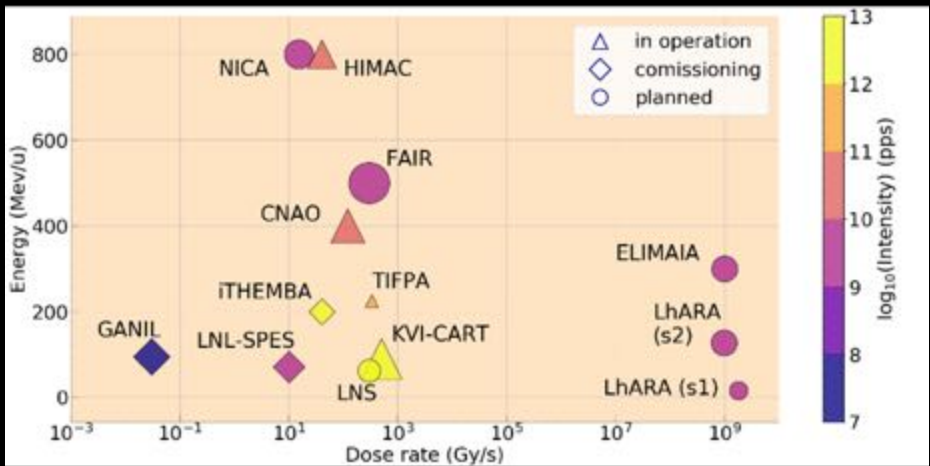
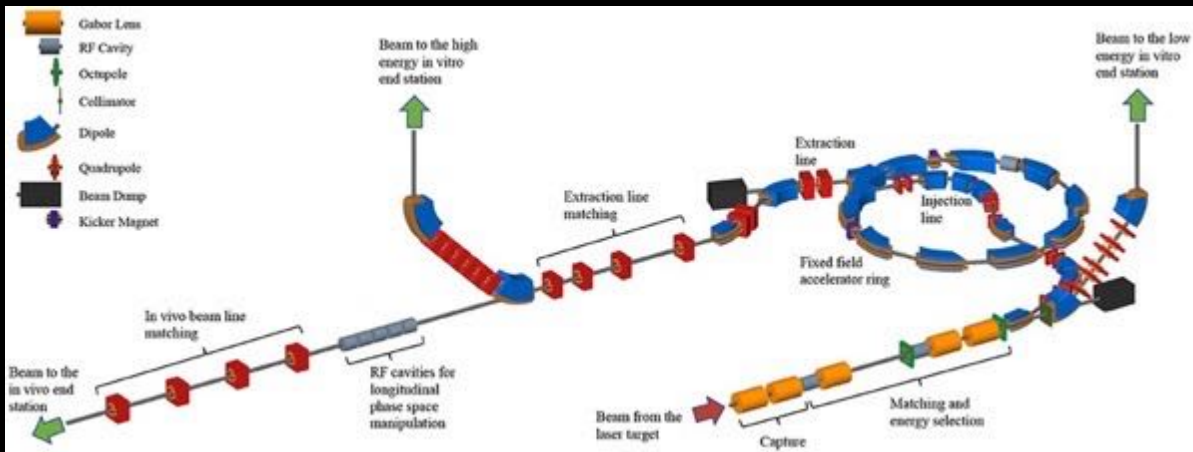
Università di Milano e sezione INFN di Milano – LASA

R. Musenich INFN-GE, L. Sabbatini LNF, S. Giordanengo e E. Fiorina INFN-TO

# Look even further

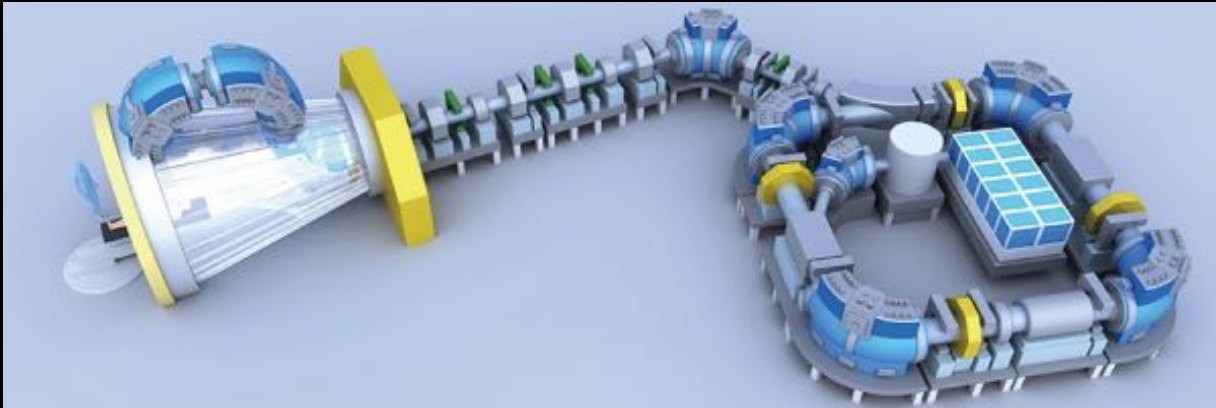


Laser-hybrid Accelerator for Radiobiological Applications



Credit: LhARA Consortium

## Quantum Scalpel



- 5th generation facility:
- Superconducting synchrotron
- Multi-ion irradiation system
- Injector with laser acceleration technology
- Rotating gantry with HTS magnets
- Microsurgery system



# New treatment modalities: Very High Energy Electrons (VHEE) + FLASH

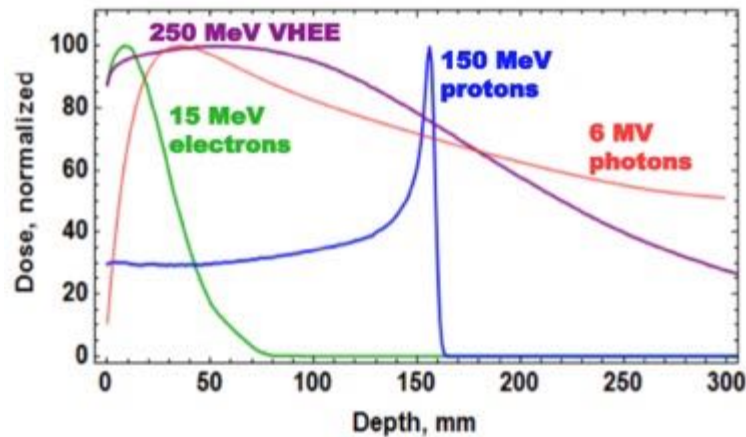
Experiments (including radiobiology) at various user facilities:

CERN Linear Electron Accelerator for Research (CLEAR)

VELA-CLARA at Daresbury Laboratory

PITZ at DESY

ELBE-HZDR in Dresden



Dose profiles for various particle beams in water (beam widths  $r = 0.5$  cm)

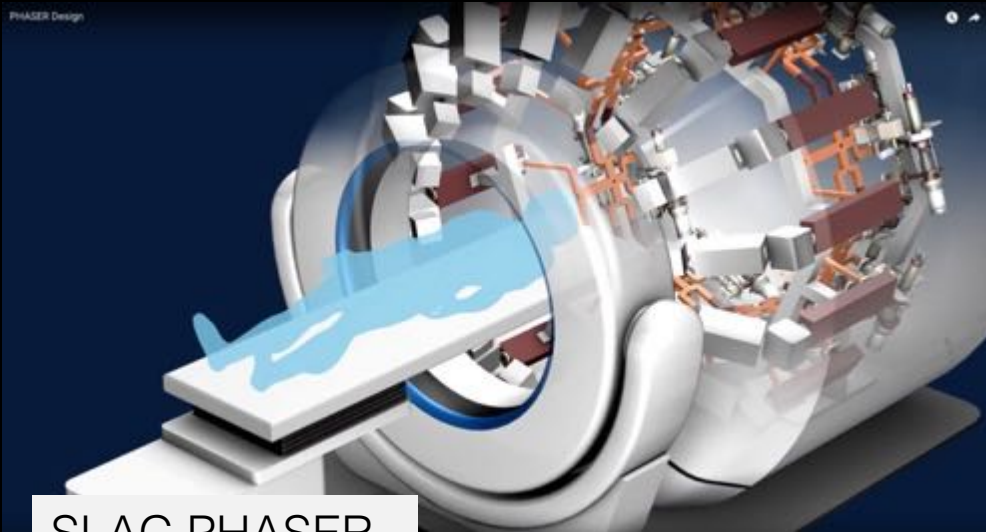


Facilities under design:

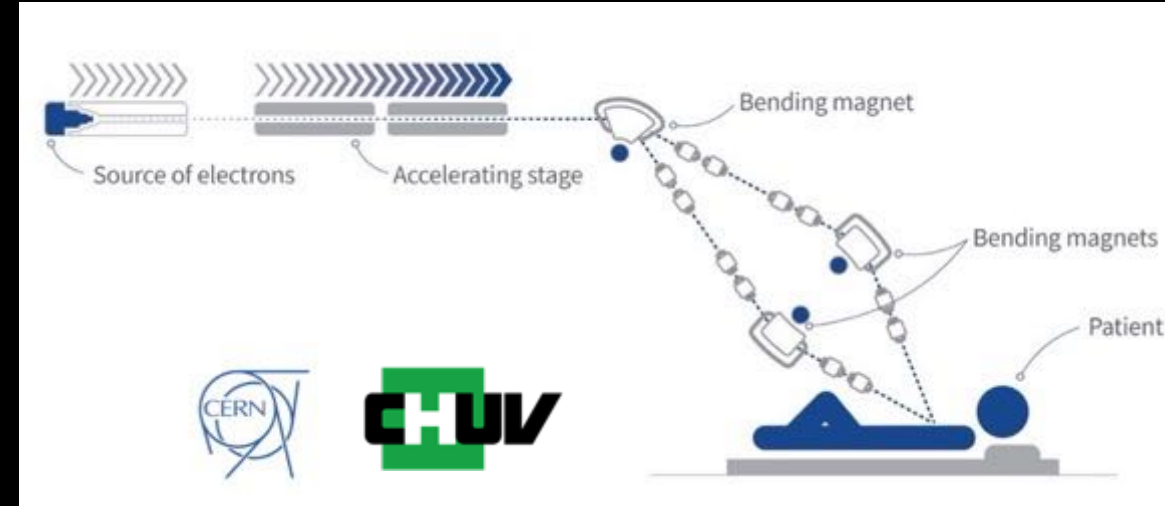
FRIDA Sapienza INFN

IDRA LOA Orsay

# VHEE FLASH clinical facilities under design



SLAC PHASER



CERN – University Hospital Lausanne (CHUV) collaboration based on the CLIC technology (see talk from S.Stapnes)

## Very intense electron beams

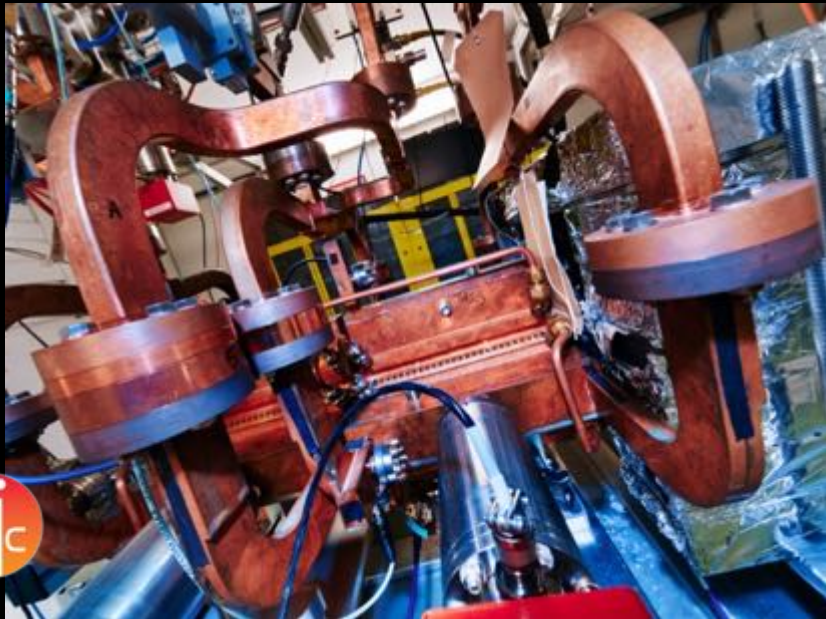
CLIC – to provide brightness needed for delicate physics experiments  
FLASH – to provide dose fast for biological FLASH effect

## Very precisely controlled electron beams

CLIC – to reduce the power consumption of the facility  
FLASH – to provide reliable treatment in a clinical setting

## High accelerating gradient

CLIC – fit facility in Lac Lemman region and limit cost  
FLASH – fit facility on typical hospital campuses and limit cost





# Radioisotopes



## Radioisotopes: The medical testing crisis

With a serious shortage of medical isotopes looming, innovative companies are exploring ways to make them without nuclear reactors.

Richard Van Noorden

11 December 2013

PDF Rights & Permissions



# Radioisotopes & Nuclear Medicine

Established isotopes → Industrial suppliers

$^{99m}\text{Tc}$ ,  $^{18}\text{F}$ ,  $^{123,125,131}\text{I}$ ,  $^{111}\text{In}$ ,  $^{90}\text{Y}$

Emerging isotopes → Small innovative suppliers

$^{68}\text{Ga}$ ,  $^{82}\text{Rb}$ ,  $^{89}\text{Zr}$ ,  $^{177}\text{Lu}$ ,  $^{188}\text{Re}$

R&D isotopes → Research labs

$^{44,47}\text{Sc}$ ,  $^{64,67}\text{Cu}$ ,  $^{134}\text{Ce}$ ,  $^{140}\text{Nd}$ ,  $^{149, 152, 155, 161}\text{Tb}$ ,  $^{166}\text{Ho}$ ,  $^{195m}\text{Pt}$ ,  $^{211}\text{At}$ ,  $^{212, 213}\text{Bi}$ ,  $^{223}\text{Ra}$ ,  $^{225}\text{Ac}$ ,...

(Courtesy Ulli Koester)



# Theranostics

<b>Tb 149</b> 4.2 m $\epsilon$ $\beta^+$ $\alpha$ 3.99 $\gamma$ 796; 165... 4.1 h $\epsilon$ $\alpha$ 3.97 $\beta^+$ 1.8 $\gamma$ 352; 165...	<b>Tb 152</b> 4.2 m 17.5 h $\gamma$ 283; 160... $\epsilon$ ; $\beta^+$ ... $\gamma$ 344; 411... $\epsilon$ $\beta^+$ 2.8... $\gamma$ 344; 586; 271...
<b>Tb 155</b> 5.32 d $\epsilon$ $\gamma$ 87; 105;... 180, 262	<b>Tb 161</b> 6.90 d $\beta^-$ 0.5; 0.6... $\gamma$ 26; 49; 75... $e^-$



H2020 PRISMAP: The European medical isotope programme (Arronax, CEA, CERN, CHUV, DTU, ESS, GANIL, GSI, ILL, INFN, IST-ID, JRC, KU Leuven, LU, MedAustron, MUI, NCBJ, NPL, PSI, SCIPROM, SCK-CEN, TUM, UIO)

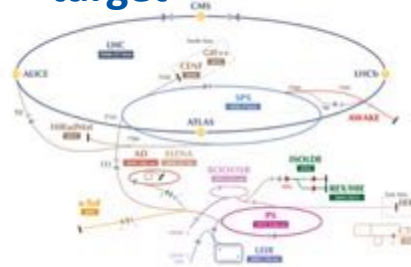
# CERN: from ISOLDE to MEDICIS



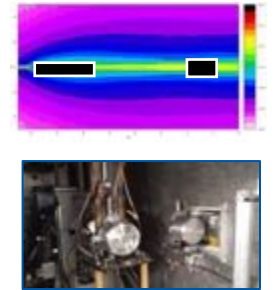
Non-conventional isotopes collected by mass separation for new medical applications

ISOLDE has been running for more than 50 years

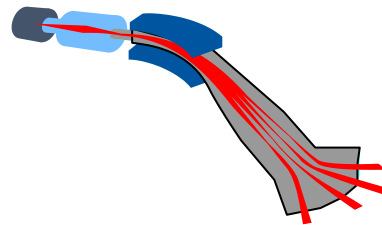
**Protons on ISOLDE target**



**MEDICIS Target Irradiation**

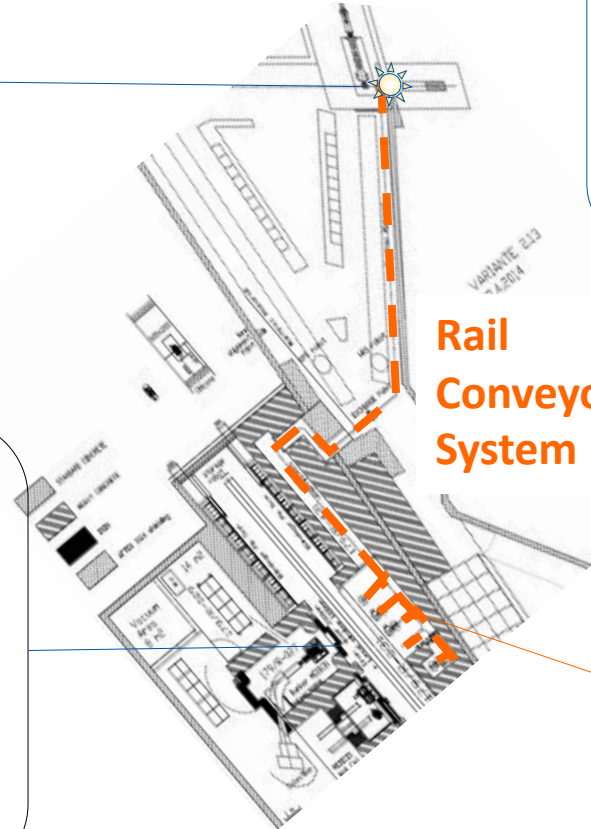


**MEDICIS Laboratory**



Isotope separation on-line (ISOL)

**Rail Conveyor System**





# CERN: from ISOLDE to MEDICIS



Year	Irradiation modes	Medical isotopes	Collected activity (MBq)
2018	CERN PSB & external irradiations	C-11, Tb-149, Tb-152, Tb-155, Tm-165, Er-169	235
2019	External irradiations	Tb-155, Er-169, Yb-175, Pt-195m	870
2020	External irradiations	Sm-153, Tb-155, Tm-167, Ac-225	540



MEDICIS run during LS2: operating with sources irradiated outside CERN.

Sources provided by MEDICIS collaborating institutes.

Mass separation at CERN MEDICIS when needed.

Purification in collaborating institutes by radiochemistry.

# SPES-Selective Production of Exotic (nuclear) Species @ LNL



## SPES- $\alpha$

production and delivery to the target of Cyclotron proton beams)



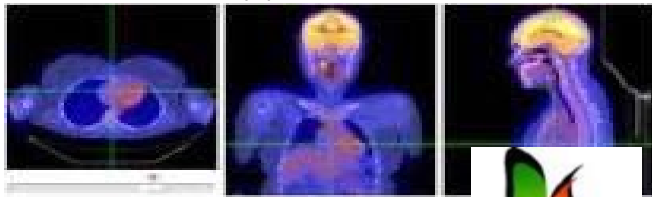
## SPES- $\beta$

ISOL facility and the acceleration of neutron-rich unstable nuclei



## SPES- $\gamma$

Radioisotopes for medical applications



ISOLPHARM & LAIRA MED



$\beta$

$\alpha$

$\gamma$

$\delta$

## SPES- $\delta$

Neutron source for applied physics and industry





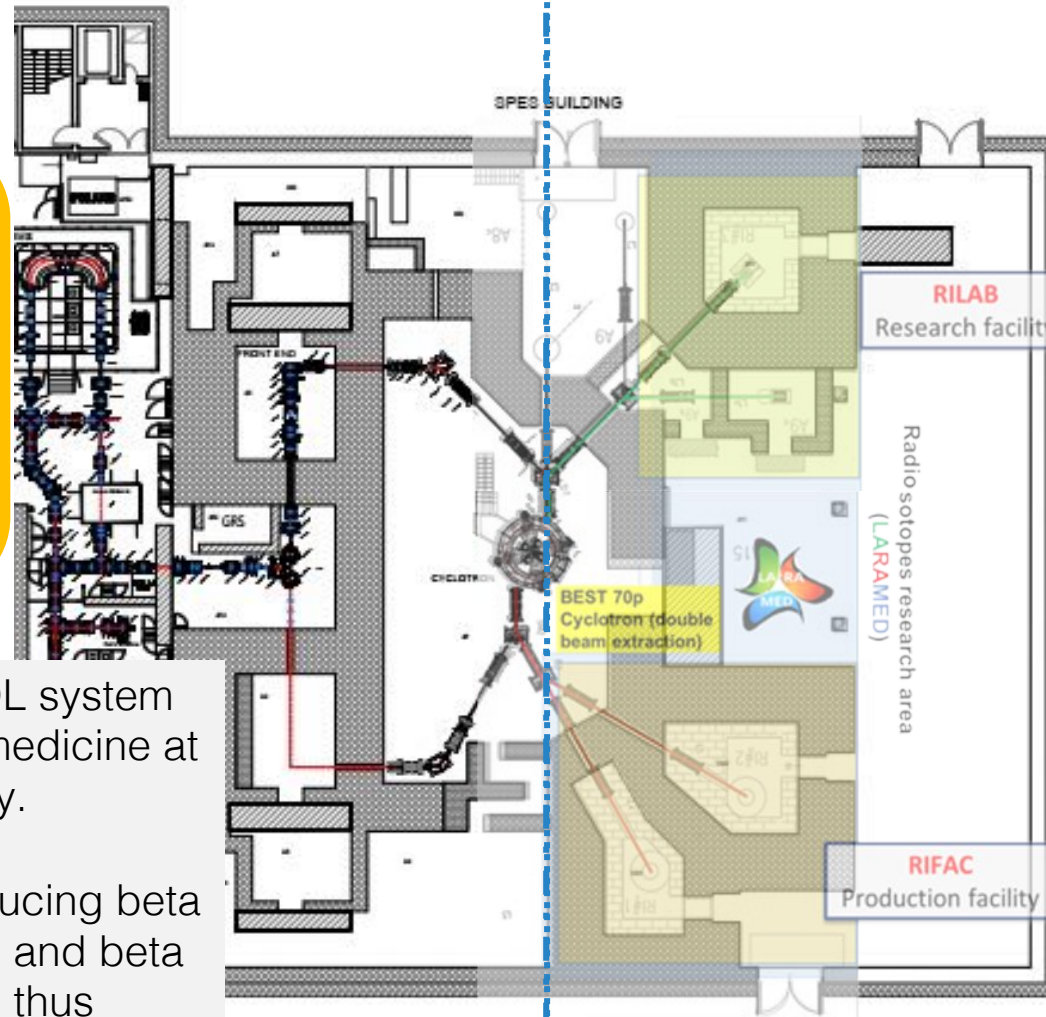
# SPES- $\gamma$ : innovative radioisotopes for medical applications

Production of radioisotopes for medical applications via **ISOL technique**

**ISOLPHARM**  
SPES exotic beams for medicine

Focused on the use of the ISOL system to produce radioisotopes for medicine at high specific activity and purity.

INFN patent «Method for producing beta emitting radiopharmaceuticals and beta emitting radiopharmaceuticals thus obtained»



Production of radioisotopes for medical applications via **direct activation**



Laboratory of Radionuclides for MEDicine

 **molecules**



Letter

## LARAMED: A Laboratory for Radioisotopes of Medical Interest

Juan Esposito <sup>1</sup>, Diego Bettoni <sup>1,2</sup>, Alessandra Boschi <sup>3</sup>, Michele Calderolla <sup>1</sup>, Sara Cisternino <sup>1</sup>, Giovanni Fiorentini <sup>2</sup>, Giorgio Keppel <sup>1</sup>, Petra Martini <sup>1,3,\*</sup>, Mario Maggiore <sup>1</sup>, Liliana Mou <sup>1</sup>, Micòl Pasquali <sup>1</sup>, Lorenzo Pranovi <sup>1</sup>, Gaia Pupillo <sup>1</sup>, Carlos Rossi Alvarez <sup>1</sup>, Lucia Sarchiapone <sup>1</sup>, Gabriele Sciacca <sup>1</sup>, Hanna Skliarova <sup>1</sup>, Paolo Favaron <sup>1</sup>, Augusto Lombardi <sup>1</sup>, Piergiorgio Antonini <sup>1</sup> and Adriano Duatti <sup>1,4</sup>

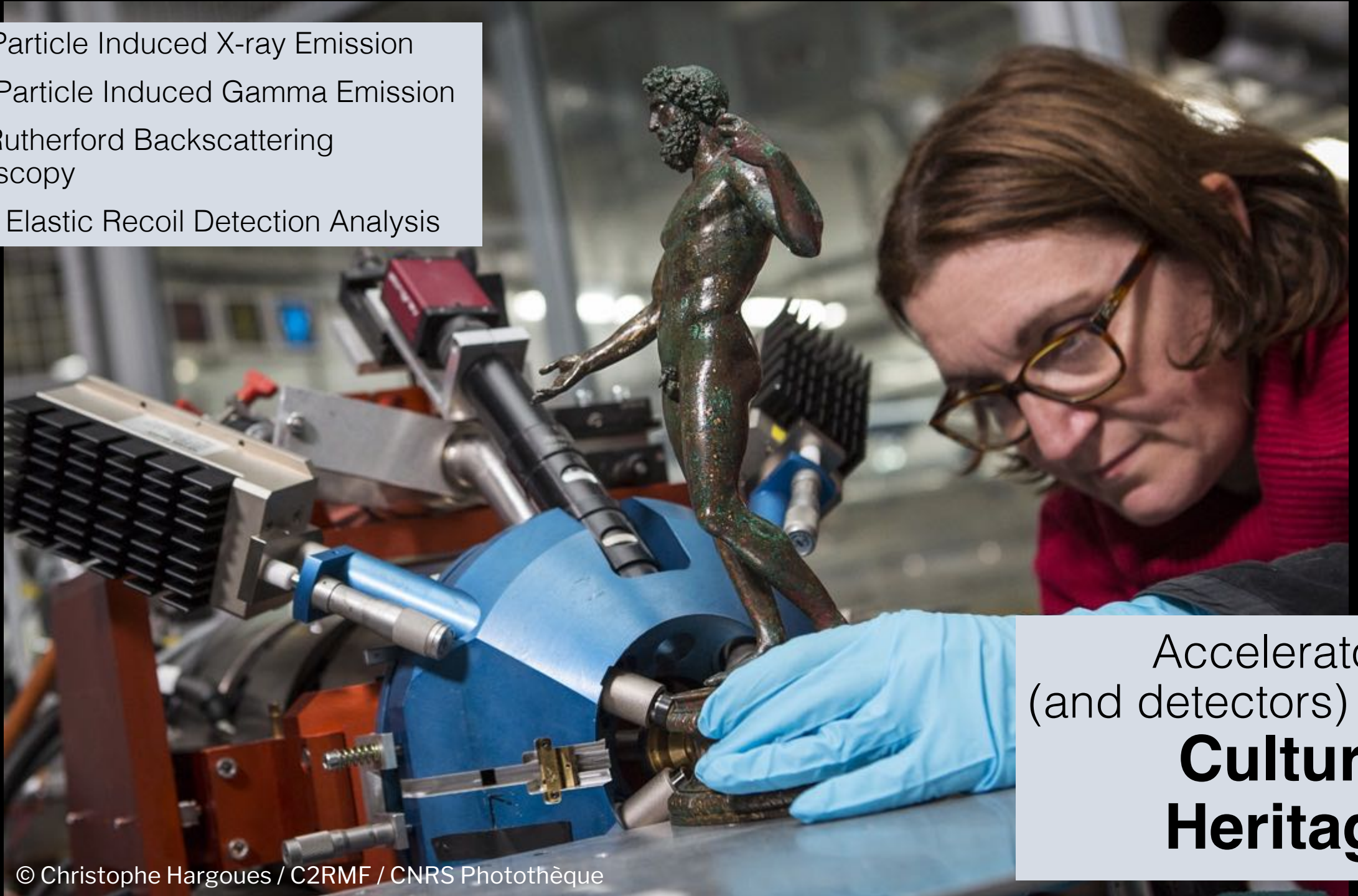
[\*] Esposito J et al., Molecules **2019**, 24, 20; doi:10.3390/molecules24010020

PIXE = Particle Induced X-ray Emission

PIGE = Particle Induced Gamma Emission

RBS = Rutherford Backscattering  
Spectroscopy

ERDA = Elastic Recoil Detection Analysis



Accelerators  
(and detectors) for  
**Cultural  
Heritage**



# New AGLAÉ – Accélérateur Grand Louvre d'Analyse Élémentaire



Yann Caradec, CC BY-NC-SA 2.0



Jean-Pierre Dalbéra [CC BY 2.0], wikimedia commons



CHRISTOPHE HARGOUES / C2RMF / AGLAE / CNRS PHOTOTHÈQUE

CENTRE DE  
RECHERCHE  
ET DE  
RESTAURATION  
DES MUSÉES  
DE FRANCE



# MACHINA

**Movable Accelerator for  
Cultural Heritage In-situ  
Non-destructive Analysis**

Construction of  
a compact,  
transportable  
accelerator



Photo: INFN





# Environmental applications

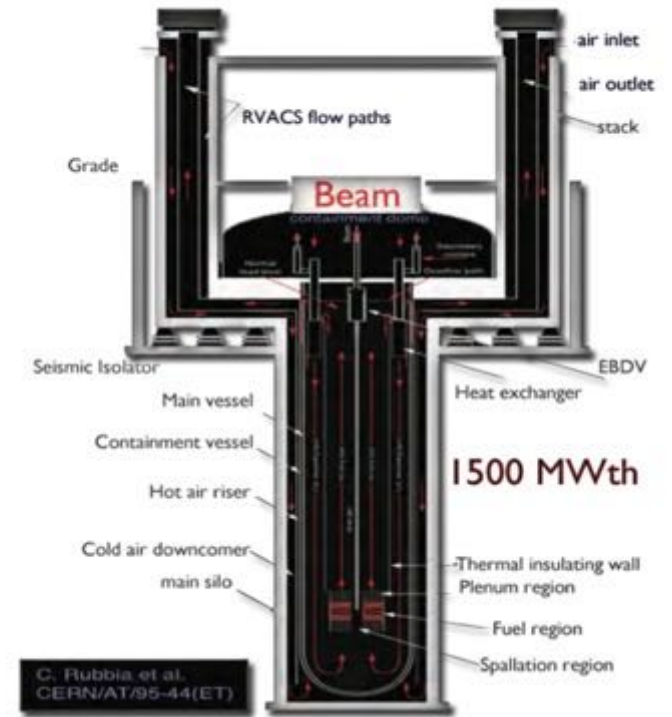
Carlo Rubbia's energy amplifier concept.

« Cleaner and inexhaustible nuclear energy production driven by a particle beam accelerator »

CERN/AT/93~47 (ET)

<https://cds.cern.ch/record/256520/files/at-93-047.pdf>

Figure 1. Carlo Rubbia's energy amplifier concept [1] [2]



(Not really HEP!)

A cruise ship emits as much sulphur oxides as 1 million cars!

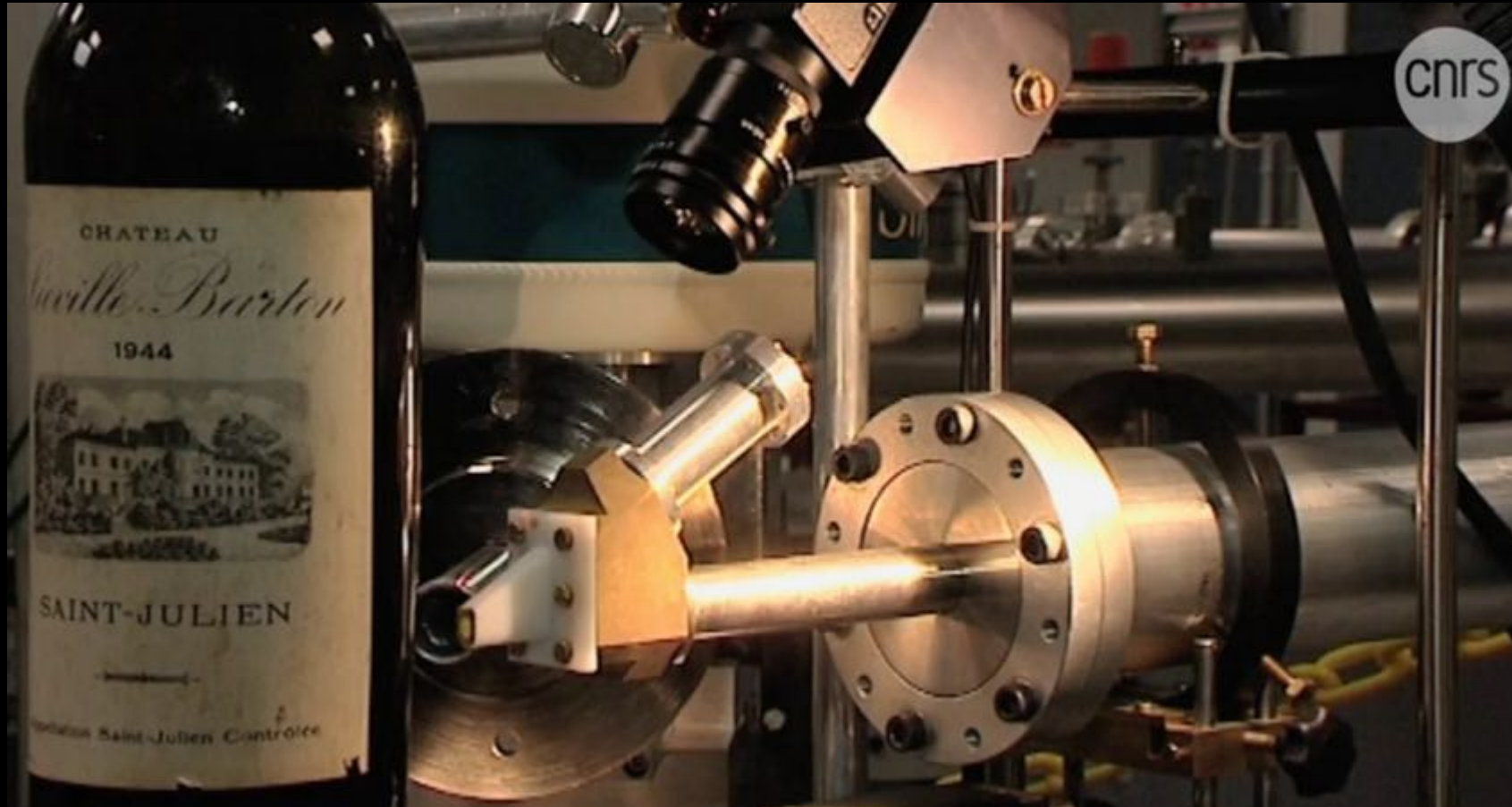
So far, technical solutions exist to reduce SO<sub>x</sub> or NO<sub>x</sub>, but there is no economically viable solution for both.

Hybrid Exhaust Gas Cleaning Retrofit Technology for International Shipping (HERTIS)

150 kV electron accelerator to break the high order molecules that are then cleaned by a water jet (scrubber).



# In vitrum veritas





# The ISEULT whole body 11.7 T MRI magnet

NEUROSPIN: a unique concept  
in neuroscience research

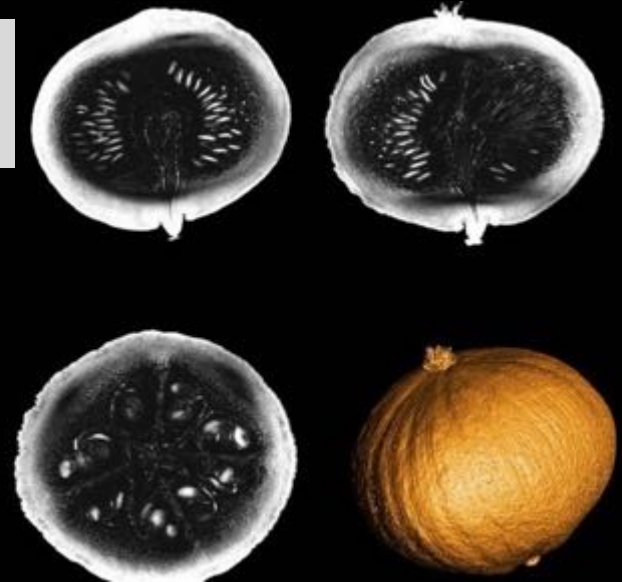


The ISEULT  
magnet -  
a French-German  
initiative

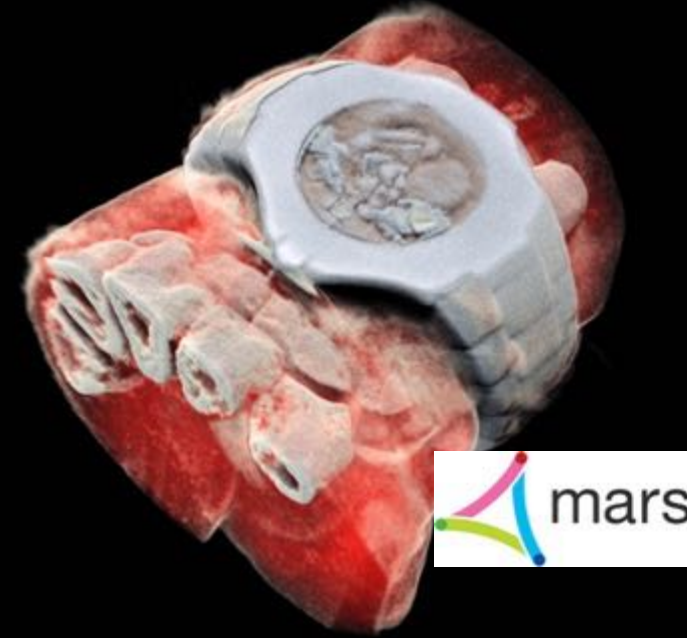
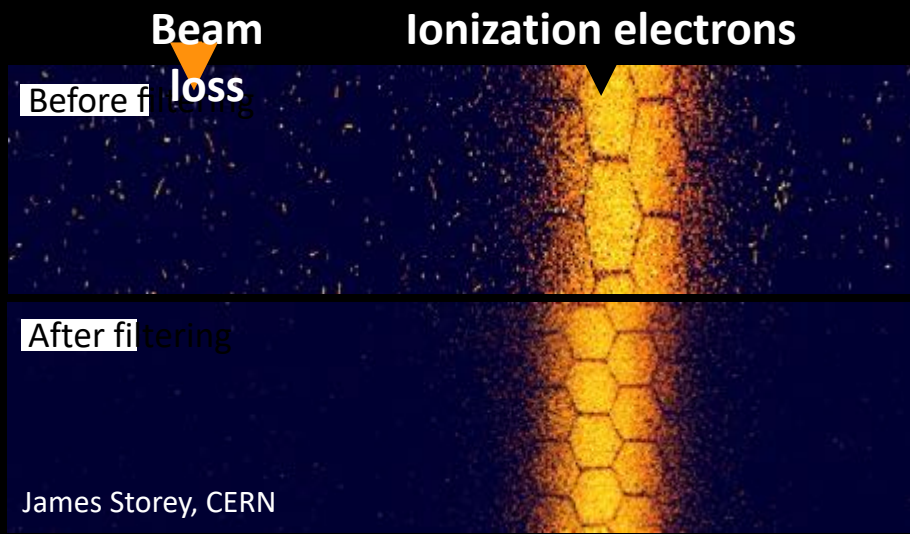
Full field of 11.72  
teslas achieved  
on July 18, 2019



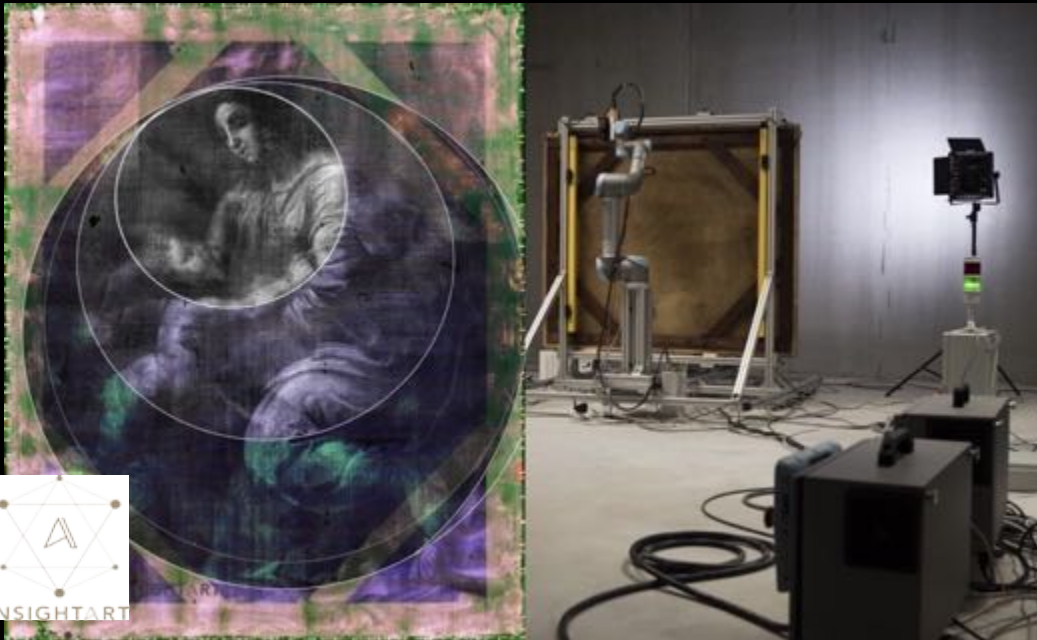
First images released  
Oct. 7, 2021







**medipix**  
collaboration



© NASA, photo ref. no. iss036e006175





## Space applications

European Space Agency

[Geant4 Space Users' Home Page](#)

[ESA Project Support](#)

[XMM-Newton Radiation Environment](#)

[Space Environment Information System \(SPENVIS\)](#)

[Dose Estimation by Simulation of the ISS Radiation Environment \(DESIRE\)](#)

[Physics Models for Biological Effects of Radiation and Shielding](#)

[Geant4 Radiation Analysis for Space \(GRAS\)](#)

[MULTi-LAyered Shielding Simulation Software \(MULASSIS\)](#)

GLAST

[Gamma Ray Large Area Space Telescope](#)

MEGAlib

[Medium Energy Gamma-ray Astronomy library](#)

## Medical applications

[G4DNA](#)

[Geant4-DNA project](#)

[G4MED](#) (in Japanese)

[Geant4 Medical Physics in Japan](#)

[G4NAMU](#)

[Geant4 North American Medical User Organization](#)

[GAMOS](#)

[Geant4-based Architecture for Medicine-Oriented Simulations](#)

[GATE](#)

[Geant4 Application for Tomographic Emission](#)

[GHOST](#)

[Geant4 Human Oncology Simulation Tool](#)

[TOPAS](#)

[Geant4 Monte Carlo Platform for Medical Applications](#)

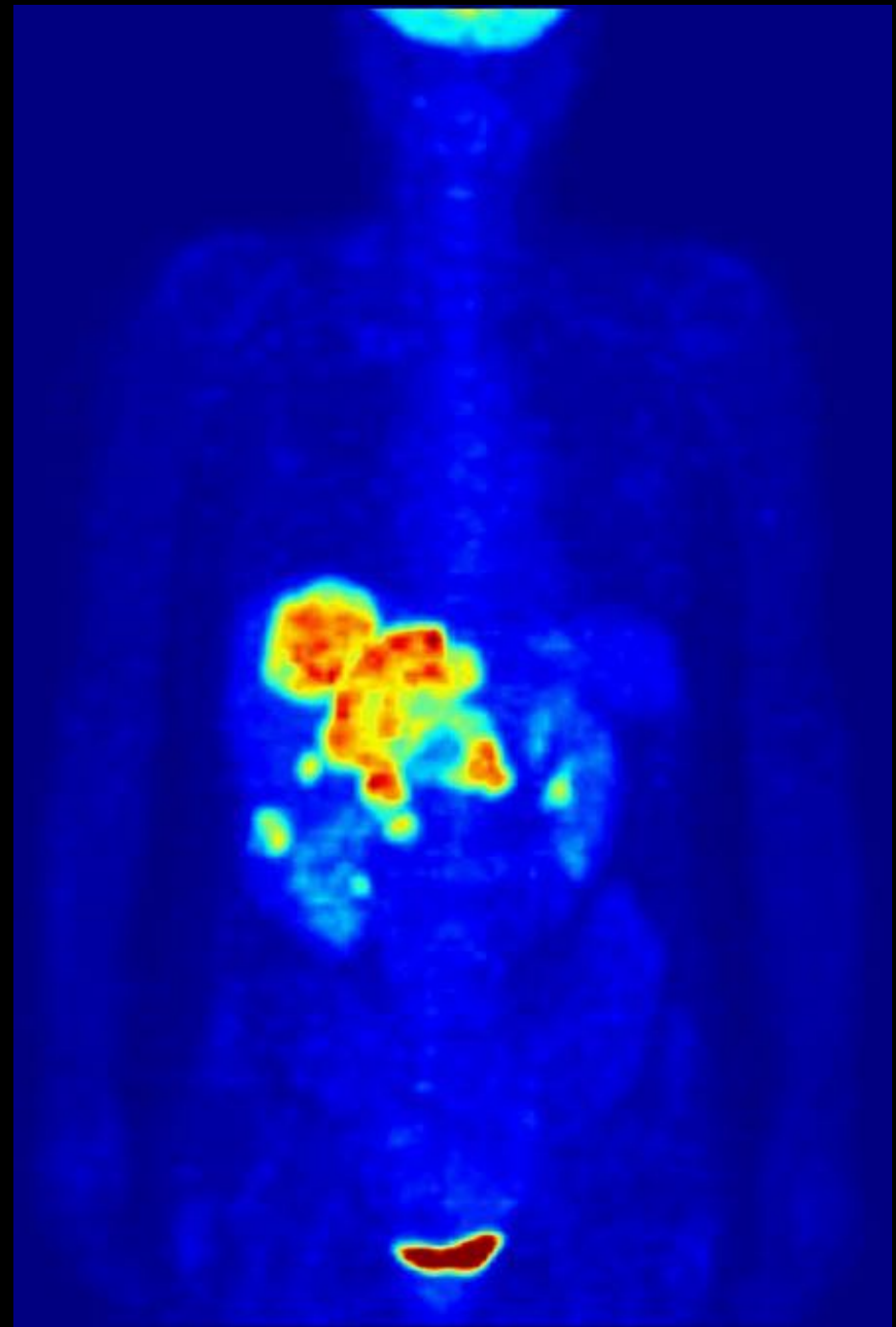
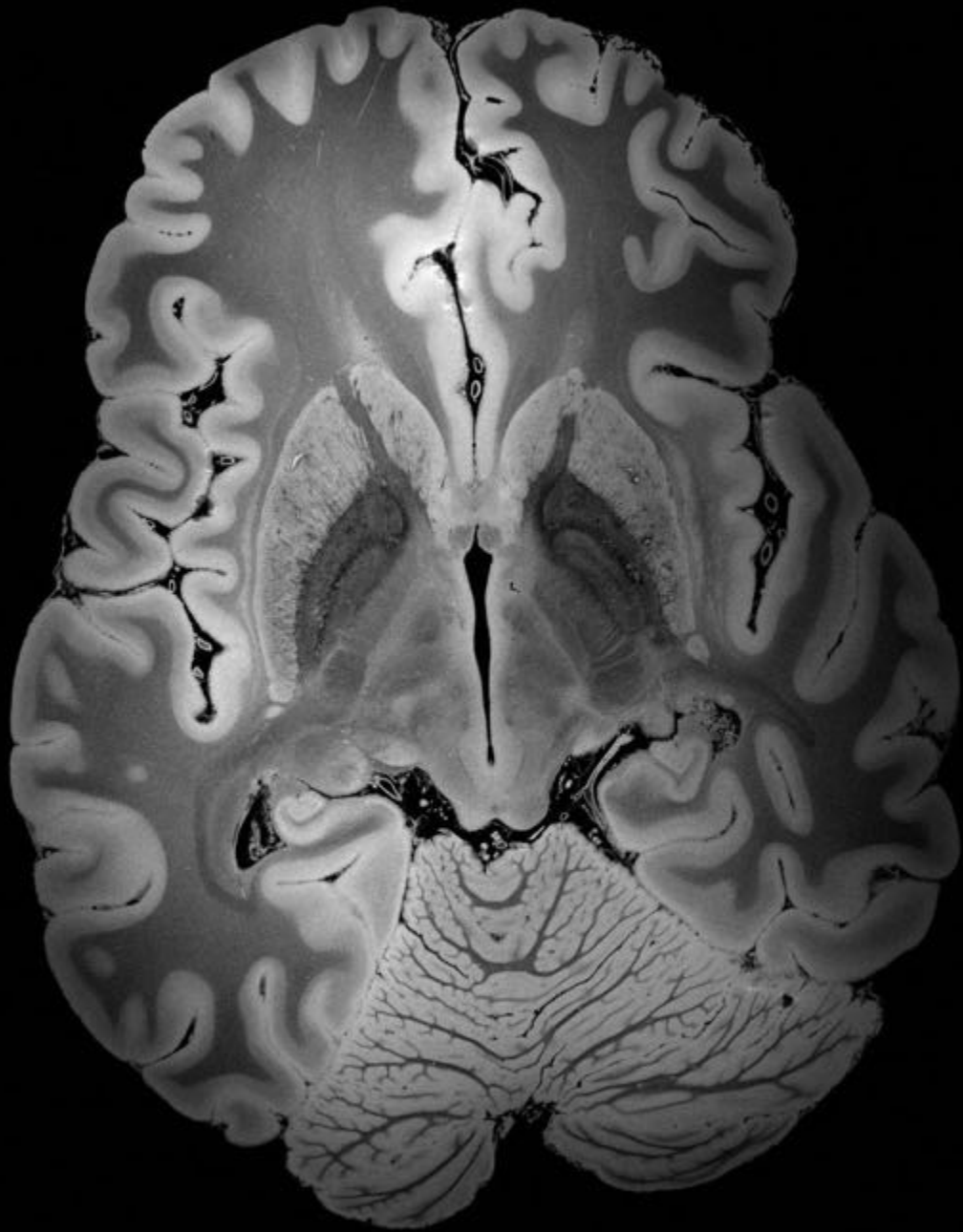
## + industrial applications

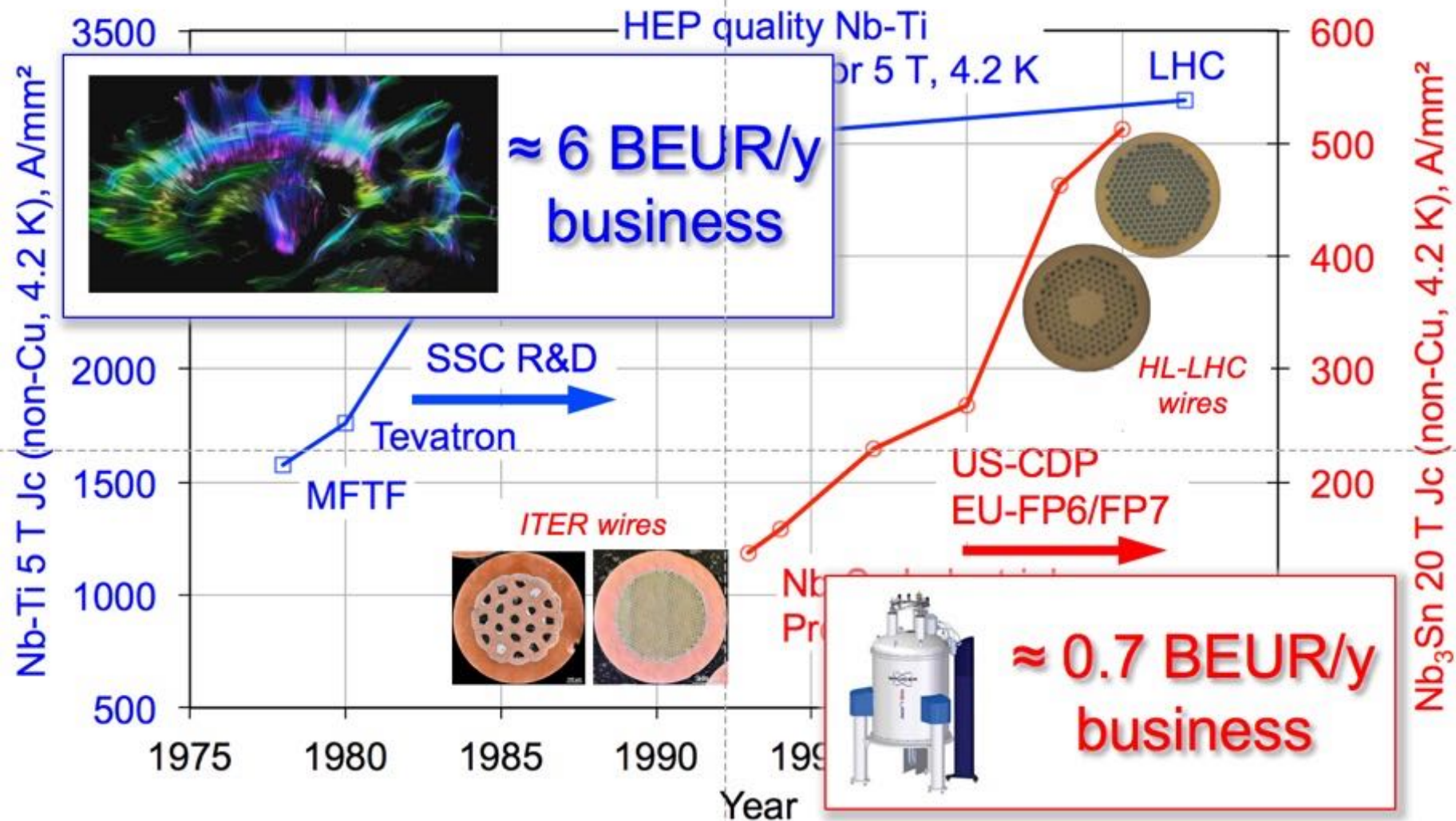
Notably, non-destructive testing

# A long and winding road...









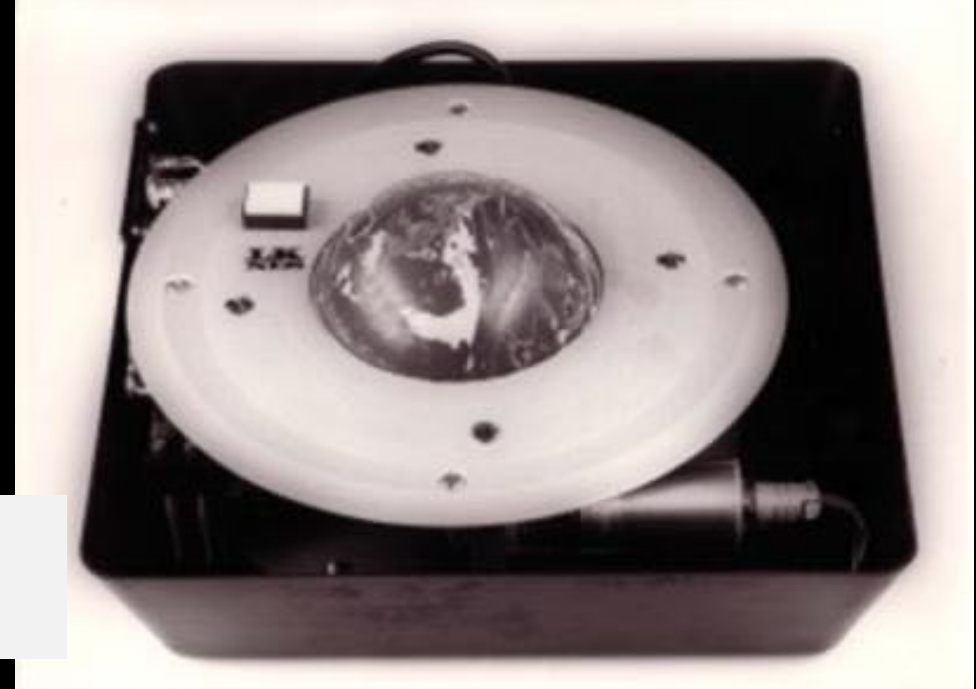
Courtesy Luca Bottura



# How do we **MAXIMISE IMPACT?**



CERN, 1970s



# The Usefulness of Useless Knowledge



ABRAHAM FLEXNER

*With a companion essay by*  
ROBERT DIJKGRAAF

In the end, utility resulted, but it was never a criterion to which his (*Faraday's, ndr*) ceaseless experimentation could be subjected.

I am not for a moment suggesting that everything that goes on in laboratories will ultimately turn to some unexpected practical use or that an ultimate practical use is its actual justification.

1939!



# THANK YOU for your attention

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# $\pi^-$ beam therapy

**1935** Yukawa theory on pi meson

**1947** Discovery of pions

**1951** Possibility of using negative pions for cancer therapy (Tobias and Richman)

**1961** Clinical use of  $\pi^-$  advocated (Fowler and Perkins, Nature 1961)

**'70-'80s** Clinical trials of negative pions at LAMPF, TRIUMF, PSI and Stanford

William T. Chu  
EO Lawrence Berkeley National Laboratory  
PTCOG From 1985 to Present and Future



*In a pilot experimental program at LAMPF's Biomedical Facility, about 250 patients were treated with negative pions for a variety of advanced deep-seated tumors. Compared to conventional x-ray therapy, pion therapy is expected to provide improved dose localization and biological effectiveness. Shown positioning a patient under the pion radiotherapy beam are (left to right) Dr. Morton Kligerman, former Director of the University of New Mexico's Cancer Research and Treatment Center, a visiting radiotherapist from Japan, and Dr. Steven Bush, formerly of the University of New Mexico. The hardware at the upper right includes a beam collimator, a dose monitor, and a device for changing the penetration depth of the pions.*

LAMPF: a dream and a gamble